

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindications: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other anti-depressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, dizziness, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect. **Adults:** Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d. adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. **Geriatric or debilitated patients:** 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) **Children:** 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

Supplied: Valium® (diazepam) Tablets, 2 mg, 5 mg and 10 mg; bottles of 100 and 500. All strengths also available in Tel-E-Dose® packages of 1000.

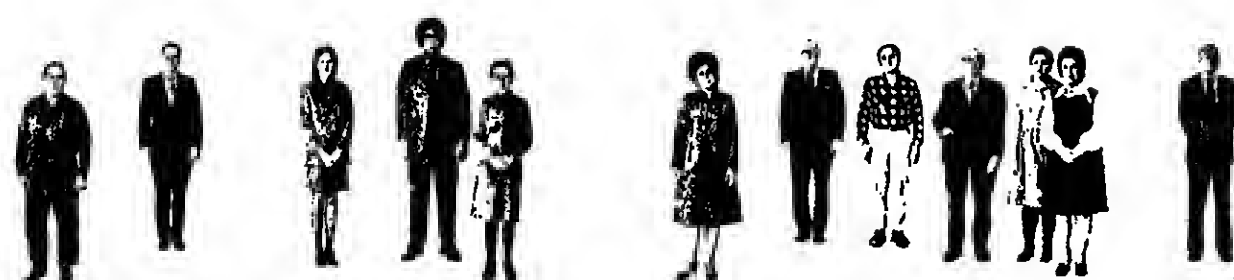
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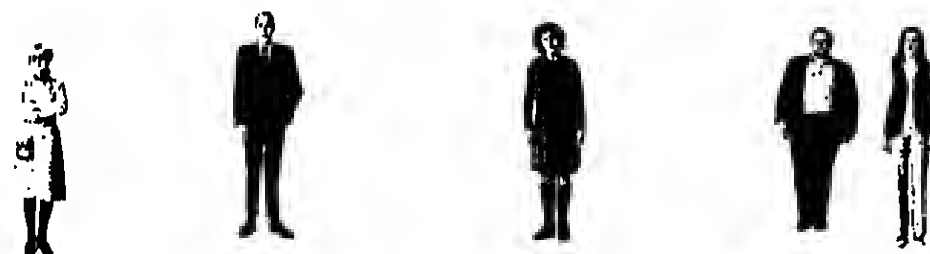
Everybody experiences psychic tension.



Most people can handle this tension.



Some people develop excessive psychic tension and need your counseling,



and a few may need counseling and the psychotropic action of Valium (diazepam).

Before deciding to make Valium (diazepam) part of your treatment plan, check on whether or not the patient is presently taking drugs and, if so, what his response has been. Along with the medical and social history, this information can help you determine initial dosage, the possibility of side effects and the ultimate prospects of success or failure.

While Valium can be a most helpful adjunct to your counseling, it should be prescribed only as long as excessive psychic tension persists and should be discontinued when you decide it has accomplished its therapeutic task. In

general, when dosage guidelines are followed, Valium (diazepam) is well tolerated (see Dosage). For convenience it is available in 2-mg, 5-mg and 10-mg tablets.

Drowsiness, fatigue and ataxia have been the most commonly reported side effects.

Valium®
(diazepam)

To help you manage excessive psychic tension

Medical Tribune

and Medical News

world news of medicine and its practice—fast, accurate, complete

Wednesday, November 29, 1972
Vol. 13, No. 46

Physicians Hail National Plan For Combating Hypertension

Medical Tribune Report

The nationwide campaign against hypertension initiated by the National Heart and Lung Institute is being hailed by physicians across the country as an important and timely project, according to a MEDICAL TRIBUNE spot check of specialists concerned with the problem.

The national program, which will be aimed at both the medical profession and the general public, was outlined by Dr. Theodore Cooper, director of the NHLI, in an exclusive interview with MEDICAL TRIBUNE published on November 1.

It calls for a coordinated effort of scientific representatives from both within and outside the Government "to establish from all the available evidence about cardiovascular disease what can be agreed upon in the areas of treatment and prevention," Dr. Cooper said.

Commenting on the program, Dr. John H. Moyer, Professor of Medicine at Hahnemann Medical College and Hospital, declared "It is timely that a major effort should be made to identify and treat patients with hypertensive disease."

Dr. John H. Laragh, Professor of Clinical Medicine and director of the Hypertension Center at Columbia-Presbyterian Medical Center, said that Dr. Cooper's "awareness of the total problem and of our ongoing capabilities to deal with it are gratifying and commendable." He suggested, however, that certain inter-

Nixon Visit to China Aids Acupuncturist

Medical Tribune World Service

HONG KONG—Business for acupuncturists in Hong Kong has increased "100-fold" since President Nixon's China trip.

Prof. Lok Yee-king, who teaches the medical needle art to Westerners, reported here that he had 500 doctors from the United States in attendance at his July lectures alone.

The professor, who is president of the Hong Kong Association of Acupuncturists, plans to expand his school if the trend continues.

mediary steps, including more research, are necessary before screening and treatment can be properly programmed.

The program was described as "a major challenge" to the health care delivery system by Dr. Edward D. Freis, senior medical investigator at the Washington, D.C., VA Hospital.

Dr. Maurice Sokolow, Professor of Medicine and chief of the cardiovascular division of the University of California at San Francisco, predicted that physicians

Continued on page 26

Pediatrician Gives Criteria To Detect Atherosclerosis

Medical Tribune Report

NEW YORK—Guidelines for identifying the child at high risk of developing premature atherosclerosis were outlined here by a University of Miami, Coral Gables, Fla.,

Lord Snow Propounds Doctrine of 'As If' On Individual Lives

Medical Tribune Report

BRONX, N.Y.—"I believe we have to act as if each individual life was significant. As if

all lives were, as religious persons have said, equal in the sight of God. As if the condition of other human beings had to be improved. As if there can come about a more desirable life for others. As if doing what we can to achieve that, we ourselves live a more desirable life.

"All that follows if we accept as a first

investigator at the annual meeting of the American Academy of Pediatrics.

Dr. Sidney Blumenthal, Professor of Pediatric Cardiology, emphasized the need for prompt evaluation of all children who have primary hyperlipidemia, hypertension, or diabetes, or who are obese. "Primary prevention of atherosclerosis is a pediatric problem," he said.

But in addition he urged physicians to take full family histories of their pediatric patients, giving special attention to questions about the occurrence in parents or other close relatives of hyperlipidemia, es-

Continued on page 31

Fetogram Shows Two Not Quite of a Kind



Diamniotic twins are seen in this fetogram taken by Dr. P. F. Wiesenhaan of the Netherlands. As well as permitting the visualization of the fetal outline and gastrointestinal tract, the fetogram stands on its own as a striking piece of photography. Indications, technique, and other examples of fetography are on page 12.

FDA Commissioner Pledges to Make 'The Voice of Science' Predominate

Medical Tribune Report

NEW YORK—Dr. Charles C. Edwards, Commissioner of the Food and Drug Administration, said here "the voice of science will be heard" at FDA to resolving issues of medicine and health care.

Warning that it has become "increasingly difficult to invoke reason, evidence, or scientific data in dealing with public

issues" and with none more so than public health, the Federal official said the nation is witnessing "a spectacle appalling to scientists—the dominance of scientific issues in nonscientific forums by nonscientists."

He then told the American Academy of Pediatrics: "I would like to say for the record and as a basis of future actions of

Continued on page 22

New Infection Control Series

What Professionals Learned About Diphtheria

The story of the still continuing 1970 diphtheria epidemic in San Antonio, Tex., is a tale of many intertwining parts—and of many medical professionals. A significant part of the story is what these professionals have learned.

Enter Dr. Alexander W. McCracken, the director of the microbiology section of Bexar County Hospital's pathology department. A British pathologist "with a primary interest in microbiology," he had

a 1958 Cyprus acquaintanceship with diphtheria that revived as cases started appearing in San Antonio in 1968. He tested

Fourth of a series.

a quick method for confirming diphtheria and now has decided opinions—some critical—about the old ones, which take so long.

Enter Charles U. Maunay, Ph.D., diagnostic bacteriologist for 15 years who had

his first taste of diphtheria in San Antonio in 1968. As associate director of the microbiology section at the time of the epidemic, he did the minute-by-minute supervision of the 14 technologists and was a prime diagnostician. Since the hospital also cultured many contacts of the diphtheria patients and since diphtheria was considered a possibility for almost every child who came to the emergency room with

Continued on page 28

Vasopressin Analogue Is Used Against Enuresis, Alcoholism

Medical Tribune World Service

Prague — A vasopressin analogue produced here, apart from its application in diabetes insipidus, is also reported to be proving useful in treating both enuresis and alcoholism.

Drs. M. and O. Birkas, of Olomouc University, Czechoslovakia, said that the drug, DDAVP (1-deamino-8-D-arginine vasopressin), has been administered for nocturnal enuresis in children from ages five to 15, with immediate success. This peptide can be pleasantly administered as nose drops or as a nasal spray, the investigators said, and they carried out a blind trial of DDAVP in 25 bed wetters by giving them nose drops at bedtime.

The induced seven or so hours of maxi-

mal antidiuresis cut down on the amount of urine formed at night, and particularly in the older group of patients, bed wetting stopped within the first two to three days of onset of therapy.

At the time of reporting, about half of the patients could be weaned away from the drug and still remain dry, whereas the remainder continued on daily application. No side effects or local irritation were observed during the test.

Urine Flow Rhythm Measured

An interesting part of the study was measurement of 12-hourly urine flow rhythms in these children prior to starting therapy. In all cases studied there was a night diuresis of highly dilute urine, which suggests that a failure of development of an endogenous antidiuretic hormone-secretion rhythm may explain part of the syndrome. The investigators failed to find any consistent psychological reason for the bed wetting in the group as a whole, but there was a tendency toward familial occurrence.

Dr. V. Holeccek, of Prague University, reported the use of the same drug as a "beer diuretic."

The beer alcoholic, he said, needs to imbibe 5-20 L. of water in a long evening's drinking at the pub in order to get his desired alcohol intake. If a family member can induce the alcoholic to take DDAVP nose drops before going to the pub, the

Medical Assistant Valued In Africa

To many citizens of developing African nations the medical assistant, whose training is half as long and one-tenth as expensive as an M.D.'s, is the medical practitioner of first contact and the major source of primary health care. Here a medical assistant from the Hudoh Health Centre in Gezireh, Sudan, measures patient's pulse rate.



WHO Photo

patient cannot excrete a water load for many hours. After drinking 2 L. of beer, signs of water intoxication begin to appear, the patient feels malaise, nausea, and weakness and goes home to sleep it off, without any really dangerous toxicity developing.

In other words, the only dangerous complication of DDAVP therapy, water intoxication—which is normally no problem because the usual patient feels no thirst—has here been put to good use.

As explained by Dr. Holeccek, the success of the treatment has little to do with the effectiveness of the drug but is reflected in the motivation of the patient and his willingness to continue to take his nose drops before a night of drinking.

Artificial Insemination: A Cup Permits Procedure To Be Performed at Home

Medical Tribune World Service

ATHENS—An insemination cup that can be fixed to the portio by vacuum in the consulting room and that avoids psychically and physically unpleasant procedures for the man in artificial insemination was described here at the third European Fertility Congress.

Dr. Kurt Semm, of the Frauenklinik und Hebammenklinik der Universität, Kiel, said that with this new method the collection of the spermatic fluid and the insemination are performed at home. The spermatic fluid is injected from a sterile syringe through a plastic tube into the insemination cup.

"In the last 20 months," Dr. Semm said, "we used the described method of insemination in 43 patients during 91 menstrual cycles (168 times). Ten patients became pregnant—of this number, five have already delivered, one had a miscarriage, and four are under surveillance."

"This kind of insemination," Dr. Semm told Medical Tribune, "maintains the personal intimacy of the couple and guarantees sterile conditions. We are convinced that this method can be particularly helpful in cases of weak spermatic fluid."

Canadian Will Undertake Study Comparing IUDs, Prostaglandins

Medical Tribune World Service

OTTAWA—A nationwide study of two methods of fertility regulation, the copper-T intrauterine device and prostaglandins, is being launched in Canada with a \$75,975 grant from the International Development Research Center here.

The one-year clinical trials will include about 1,000 Canadian women for each of the two studies in university medical centers across Canada.

Dr. Yves Lefebvre, of the University of Montreal, will be in charge of the copper-T study, and Dr. R. A. H. Kinch, of McGill University, in charge of the prostaglandins study.

Electron Microscope Magnifies by a Million

Medical Tribune Report

BETHESDA, Md. — The world's first electron microscope for biomedical research capable of magnifying specimens 1,000,000 times has been put into operation at the University of Wisconsin, it was announced by the Division of Research Resources of the National Institutes of Health.

The 1,000,000-volt facility is located in the Animal Sciences Building on the university campus in Madison.

At Boulder, Colo., the second 1,000,000-volt electron microscope facility devoted solely to biomedical research will soon be put into operation in the Molecular Cellular and Developmental Biology Building at the University of Colorado.

The two facilities, supported by grants totaling \$1,700,000 from the Division of Research Resources, will offer three features considered critical for further in-depth biomedical cell research—greater specimen penetration, reduced specimen damage, and greater image resolution.

According to Hans Ris, Ph.D., program director of the University of Wisconsin facility, one of the major advantages of the new microscope is the possibility of obtaining images with high resolution of much thicker specimens than is currently feasible.

"For instance, intact cells or sections

of plastic-embedded cells 1 or 2 micrometers thick show detail to about 20 microns with excellent contrast on the 1,000,000-volt microscope," he said.

Dr. Ris, a cytologist who has been studying chromosomes for some 33 years, feels that with the use of the new microscope he will be moving closer to his goal of unraveling the mystery of the inner workings of chromosomes. He is particularly following the DNA fiber, "which probably continues through the whole chromosome."

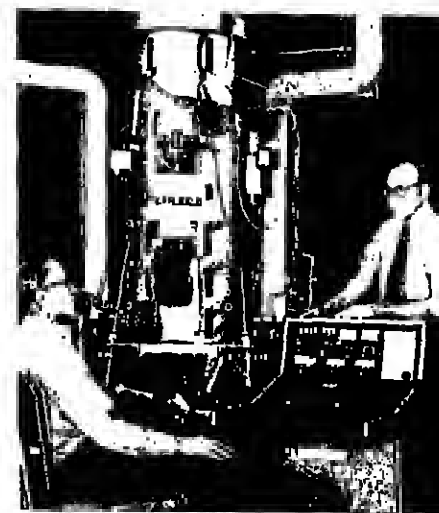
Will Allow Close Study

The resolution of the electron microscope will allow, for the first time, detailed study of intact cells or cell organelles.

"The great depth of field of the electron microscope allows stereoscopic imaging through specimen tilting," Dr. Ris explained. "This provides three-dimensional pictures never before achieved."

The gigantic instrument at the University of Wisconsin weighs 28 tons and is mounted on a 60-ton cement block. To eliminate vibration, the 88-ton installation floats on three compound plastic bags inflated by compressed air. Manufactured by Allied Electrical Industries of Essex, England, the instrument is installed in a space measuring 40x20x30 feet.

The instrument nearing completion at the University of Colorado has been con-



At the University of Wisconsin's new electron microscope are Hans Ris, Ph.D., program director, seated, and physicist-in-charge Dale Johnson, Ph.D.

stricted with the same general specifications by Jeolco, Inc., of Japan. Keith R. Porter, chairman of the Department of Molecular Cellular and Developmental Biology, is the program director for the facility.

Dr. Porter intends to concentrate his studies on the organization of the nucleus—"an area which we know nothing about, yet it's responsible for the organization, shape, and function of the cell center."

Heroin Addicts: Growth Pattern Seen Reversing

Medical Tribune Report

WASHINGTON—A reversal of a six-year pattern of progressive growth in the number of new heroin addicts is indicated by information available to the Special Action Office for Drug Abuse Prevention. Dr. Jerome H. Jaffe, director, said in a statement here.

The indications are that, for the country as a whole, the total of new addicts in 1971 "may prove to be less" than that in 1970, Dr. Jaffe said.

"New heroin users tend to communicate their behavior giving rise to still more new heroin users," he said. "On this basis, simply holding constant the number who become new users each year would have been a substantial achievement, given the large number of users already present by 1969."

A sharp and rapid growth in the number of heroin addicts began about 1965 and continued at an accelerating rate through 1969, Dr. Jaffe said. He described those years as "the epidemic years" and estimated that the heroin addict population in the U.S. doubled during those years.

Mathematic Formula Employed

Studies published by the Bureau of Narcotics and Dangerous Drugs estimate the number of addicts using a mathematic formula applied exclusively to arrested addicts, he said.

The information available to his office is "not inconsistent" with these studies, Dr. Jaffe pointed out.

"Equally important is the fact that the growth of treatment alternatives over the past three years has been unprecedented," he said.

"In 1969 there were only 16 federally supported programs able to provide care to about 5,000 drug users at any given time. By June, 1971, this had grown by more than 300 per cent to 16,000 in treatment at any given time with an estimated annual capacity of 27,000."

Dr. Jaffe noted that in June, 1971, President Nixon made the coordination and growth of this effort a personal concern by moving its direction into the Executive Office of the President.

"Since that time, the capacity of federally operated or supported treatment programs has almost quadrupled and more treatment capacity has developed than in the preceding 50 years," he said. "We have now reached the point where we can provide treatment to more than 60,000 drug users at any given time with an estimated treatment capacity of well over 100,000 drug users each year."

This growth does not include the substantial support given to state and local treatment programs over the last three years through block grants and cost sharing arrangements, Dr. Jaffe noted.

Three months ago, the chief executive asked Congress for resources to expand treatment capacity further to a point where Federal, state, and local programs will be able to treat more than 250,000 drug users each year, he added.

ECTOPIC BEAT

"In reply to your editorial on Mandatory Continuing Education, your crystal ball must be tuned to a different wave length than most pharmacists I have talked with on the aspect of continuing education."

—Rocky Mountain Druggist. And what's more, those electronic crystal balls pick up a lot of static. (Regular beat continues in Medical Tribune, page 31.)

Pancreas Transplants Called Useful in End-Stage Diabetes

Medical Tribune Report

SAN FRANCISCO — Encouraging preliminary results with pancreas transplantations using ureteral exocrine drainage have been obtained in a small number of diabetics with end-stage disease, according to a surgical team at Montefiore Hospital in New York.

Dr. Marvin L. Gledman, Professor of Surgery and chairman of the department at the Albert Einstein College of Medicine, told the Clinical Congress of the American College of Surgeons here that of four patients who received a transplanted pancreas without accompanying duodenum, three have survived, two with functioning glands.

The patients, all in their 20s or 30s, Dr. Gledman commented, had severe intractable disease. All had been juvenile diabetics and had renal disease, neuropathies, and visual difficulties. Such patients normally, he noted, "have a very limited outlook."

Team's Technique Outlined

Dr. Gledman outlined the team's technique as necessitating transfer of a segment of the pancreas and anastomosing the ureter, otherwise unused in the patients because of renal dysfunction, to the pancreatic duct.

There was no evidence, he said, of damage to the urogenital system caused by the excretion through it of pancreatic digestive fluids in any of the patients or in 10 dogs followed for up to a year, as evidenced by appearance or histologic section. The sole complication in the urogenital system, he indicated, was a loss of bicarbonate to the urine, requiring some bicarbonate supplementation.

The use of the ureter for drainage of pancreatic exocrine flow, Dr. Gledman observed, "enormously amplifies the transfer." It avoids bowel anastomosis, external drainage, or any surgical invasion of the peritoneal cavity, he remarked.

The current procedure, he said, appears especially promising, as it does not include duodenal transplant. The high rejection rate and the technical difficulties to prevent pancreas transplants, he noted, appeared to relate chiefly to the transfer of a section of the duodenum with the pancreas and its duct for exocrine drainage, rather than the pancreas proper.

Of the two patients with functioning transplants, Dr. Gledman reported, one has survived for four months and has required no insulin since the operation. The other, who also received a kidney transplant, has survived nine months, requiring no insulin in the initial postoperative period. However, she sustained pancreatic and kidney damage after failing to take her immunosuppressives for a short period and now requires some insulin, approximately one-third of her preoperative dosage.

For end-stage diabetics, Dr. Gledman suggested that pancreas transplantation with ureteral drainage "is at this time the available mechanism that seems to solve the problem." He added that "we think if it holds up in this rather desperate group, that we could extend it."

He cautioned, however, that the procedure is probably not indicated beyond those diabetics with renal failure. A ureter from a nonfunctioning kidney is needed, and even though the pancreas does not

Family Practice Program Drawing Young Doctors

Medical Tribune Report

KANSAS CITY, Mo. — The annual survey of family practice residency programs showed that 1,015 young physicians are taking part in the programs, almost double the number a year ago, the American Academy of Family Physicians said here. Three years ago, there were 20 approved programs, the AAFP noted. There are now 107.

The survey also showed that 81 per cent of the available first-year family practice residency slots are filled, increasing by more than 10 per cent the figure in 1971. This percentage of filled first-year slots, it was noted, is higher than that for most other medical specialties.

seem to be as antigenic as other organs, thus requiring comparatively low levels of immunosuppressives when transplanted, "it is a lot easier to control insulin than azathioprine."

Coauthors were Drs. Michael Gold, John R. Whitaker, and Frank J. Veith, of the Department of Surgery.

Fourth of Hospital Patients In Cities Termed Alcoholics

Medical Tribune Report

NEW YORK — The American Hospital Association, declaring that 25-30 per cent of all adult medical-surgical patients in metropolitan hospitals, regardless of diagnosis, have been found to be suffering from alcoholism, has announced it is undertaking a nationwide program to educate hospital personnel in treating alcoholics.

The A.H.A. hopes to "break down resistance by many doctors and hospitals to admitting acutely ill alcoholics as inpatients and to tie in the 6,000 voluntary hospitals with other community resources that will help the alcoholic to get and stay sober."

The association president, Alex McMahon, observed that although more hospitals are now treating alcoholics than were a few years ago, "many professionals still believe the alcoholic is a nuisance, not a sick person."

"Studies conducted by the association," he said, "show that the alcoholic is not disruptive or unmanageable or needs spe-

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CLINICAL NEWS NOTE: "I am not speaking . . . of administering an experimental drug to a patient who is not capable of giving his own consent. These are suggestions that only you—organized medicine—can answer." (Dr. Charles C. Edwards, page 1.)

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HYPERURICEMIA

Treatment of gout-part II



The Consultant

DR. JOHN H. TALBOTT
Clinical Professor of Medicine,
University of Miami School of Medicine,
Miami, Fla.

When hyperuricemia in a gouty patient has been brought down to normal levels, is it advisable to discontinue prophylactic colchicine?

In my two decades of experience with a combination of prophylactic colchicine and probenecid and thoroughly satisfactory inhibition of attacks of acute arthritis, most patients prefer to continue the colchicine and probenecid daily and indefinitely. There have been several instances in which patients well controlled on prophylactic

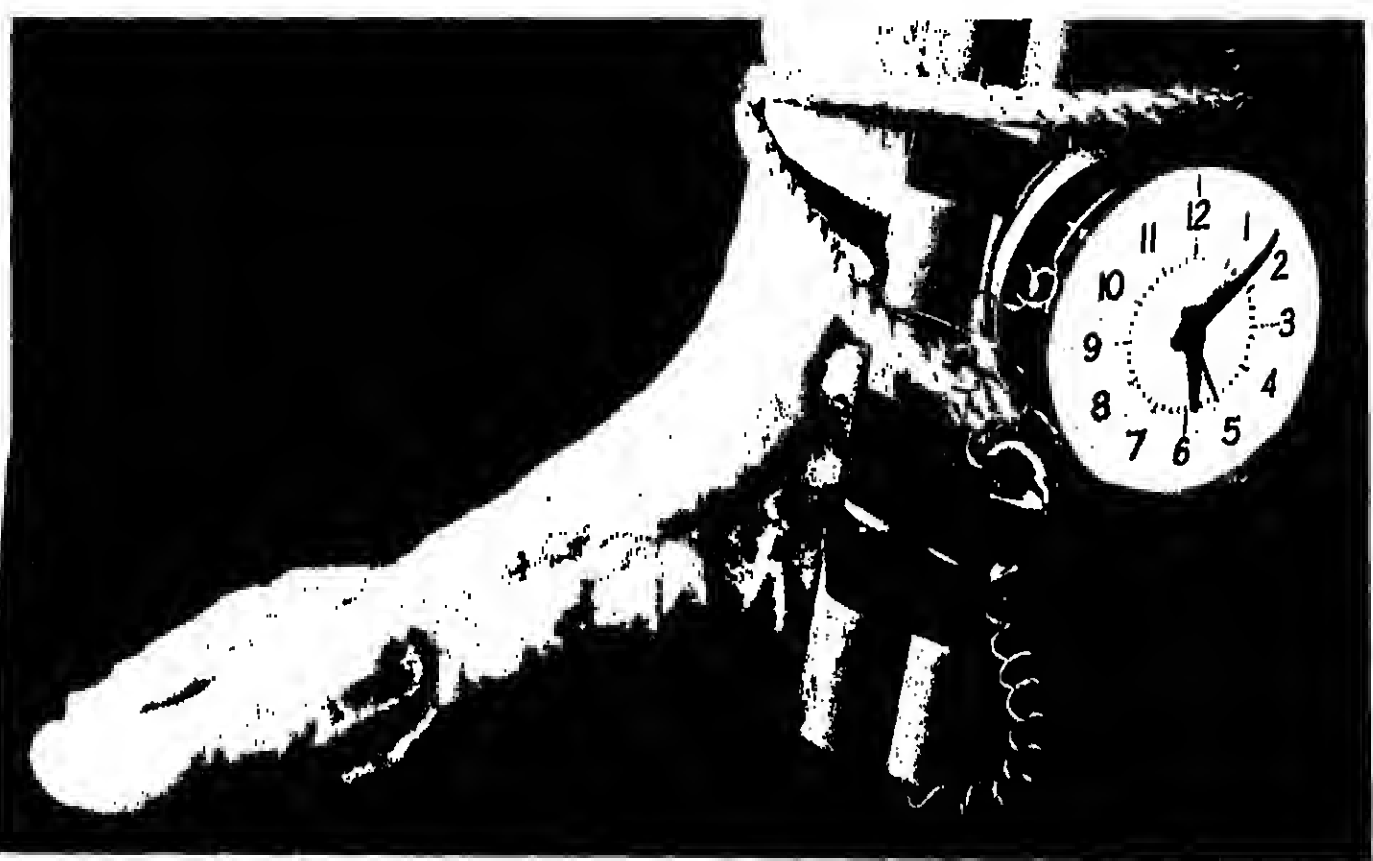
lactic medication have, after several years, either because of their belief that they may stop the medication or upon advice of their physician, discontinued colchicine. Although I do not have the precise figures I would predict that at least two-thirds of these patients experience a return of symptoms sometimes within a few days, sometimes within a few weeks, several only after several months. Each of these who experiences a return of acute arthritis is then convinced of the value of daily medication. And finally I have a few patients whose attacks were mild and who suffered not more than two or three acute but mild

episodes over a period of a similar number of years who have stopped all medication after a year or more and have done very well.

It seems to be that if a patient wishes to go off medication having been symptom-free for a long period of time on prophylactic medication, he can then determine for himself, upon the advice of his physician, whether he should discontinue medication indefinitely or at least for a period of time.

Now that several agents are available to treat acute gouty arthritis, how do you rank them in order of preference?

This cannot be answered in a single sentence. The severity of the disease is one of the determining factors. All patients with moderate (two or more acute attacks of gouty arthritis per year) should be on daily colchicine, one or two tablets every day, together with a similar number of tablets of probenecid or allopurinol. All patients with severe tophaceous gout should probably be on two or three tablets of colchicine, two or three tablets of allopurinol, and two or three tablets of probenecid daily plus a high fluid intake. I think it makes little difference for the patient



rheumatoid arthritic blowups...Tandearil[®] oxyphenbutazone NF Geigy

Tablets of 100 mg.
Important Note: This drug is not a simple analgesic. Do not administer casually. Carefully evaluate patient before giving treatment and keep them under close supervision. Obtain a detailed history, and complete physical and laboratory examination (complete hemogram, urinalysis, etc.) before prescribing and at frequent intervals thereafter. Carefully select patients, avoiding those responsive to routine measures, contraindicated patients, or those who cannot be observed frequently. Warn patients not to exceed recommended dosage. Short-term relief of severe symptoms with the smallest possible dosage is the goal of therapy. Dosage should be taken with meals or a full glass of milk. Patients should discontinue the drug and report immediately any signs of: fever, sore throat, oral lesions (symptoms of blood dyscrasias); dyspnea, epigastric pain, symptoms of anemia, black or tarry stools or other evidence of intestinal ulceration or hemorrhage, skin rashes, abnormal weight gain or edema. A one-week trial period is adequate. Discontinue in the absence of a favorable response. Restrict treatment periods to one week in patients over sixty.
Indications: Acute gouty arthritis, rheumatoid arthritis, rheumatoid spondylitis.
Contraindications: Children 14 years or less; senile patients; history of symptoms of C.I.; inflammation or ulceration including severe, recurrent or persistent dyspepsia; history of or presence of drug allergy; blood dyscrasias, renal, hepatic or cardiac dysfunction; hypertension; thyroid disease; systemic edema; glaucoma and any other gland enlargement due to the drug polymyositis (rheumatoid and lamprophagocytic arthritis) and other potent rheumatoid arthritis, or long-term anti-coagulant therapy.
Warnings: Age, weight, dosage, duration of therapy, side effects of concomitant diseases and concurrent potent chemotherapy affect in degree of toxic reactions. Carefully monitor and observe the individual patient, especially the elderly (over 60 years and over) who have increased susceptibility to the toxicity of the drug. The lowest effective dosage. With initially unpredictable benefits against potential risk of severe, even fatal, reactions.

The disease condition itself is unrelated by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, dermatitis, and G.I. tract has occurred. The drug may potentiate action of insulin, sulfonylureas, and sulfonylurea-type agents. Carefully observe patients taking these agents. Nontoxic and toxic gallstones and myxomas have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant side effect. A complete ophthalmologic examination, including of angles or lens in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.
Precautions: The following should be noted: complete history of disease being treated and detection of earliest signs of adverse reactions; complete physical examination including check of patient's weight; complete weekly laboratory studies, particularly for the elderly or an elderly patient; complete laboratory studies, particularly for the elderly or an elderly patient; complete laboratory studies, particularly for the elderly or an elderly patient; complete laboratory studies, particularly for the elderly or an elderly patient.

dominal distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult O.I. bleeding, thrombocytopenia, pancytopenia, leukopenia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), polychemia, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrolytic epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angitis (polyarteritis), anaphylactic shock, urticaria, arthritis, fever, rashes (allergic reactions), renal failure with azotemia, glomerulonephritis, acute tubular necrosis, glomerulonephritis, bilateral renal cortical necrosis, renal stones, renal artery stenosis, ureteral obstruction with ureteral dilation, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with mural necrosis, pericardial granulomas, aggravation of latent arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, diabetes mellitus, toxic goiter, acceleration of hyperthyroidism and hypothyroidism (cause relationship not established), agitation, confusion, delirium, lethargy, CNS reactions associated with overdosage, including convulsions, apoplexy, psychosis, depression, headache, hallucinations, dizziness, vertigo, coma, hyperreflexia, incontinence, ulcerative stomatitis, salivary gland enlargement, (15194-16-20-2)

Next In Consultation

DR. GEORGE WEIG, Professor, University of Chicago Schools of Cytology and Cytochemistry, Chicago.

...will answer such questions as:
● Should Papaincolone smears of the cervix be made in all women once a year, or should distinctions be made according to race?
● How do you view the oral contraceptives regarding the question of their incidence of thromboembolism, hypertension, etc.
● What is the status of estrogen therapy for menopausal women?

with wild gout (less than one attack per year) whether colchicine plus allopurinol or colchicine plus probenecid are prescribed. All acute stage farmers should be on allopurinol. Patients with well-developed renal disease will receive more benefit from colchicine and allopurinol than from colchicine and probenecid.

What determines a transition from hyperuricemia to attacks of arthritis?

I can only guess at this question. I believe that acute attacks are partially based upon the duration and the degree of hyperuricemia. Of course, the administration of a thiazide preparation in a normal or hyperuricemic patient enhances the probability of an acute attack.

What emphasis do you place on diet in treatment of gout?

It has never been my practice to prescribe diets for any gouty patient except for a caution regarding a minimal intake of liver, kidney, and sweetbreads and, of course, with well-developed renal disease a low-protein diet. Most patients with gout eat a normal American diet, are allowed alcoholic beverages within the restrictions of their social mores, and in every way are entitled to the amenities of life.

M.I.T. to Advise Nations On Malnutrition Problems

CAMBRIDGE, MASS.—A multidisciplinary approach to the problems of malnutrition in low-income countries will be made in a new three-year program to be conducted at the Massachusetts Institute of Technology under a \$230,000 grant from the Rockefeller Foundation.

Approaches up to now have "generally been limited in scope and effectiveness," said F. James Levinson, Ph.D., former chief, Nutrition Branch, United States Agency for International Development, and director of the program.

"Therefore, we expect to involve faculty and students from many of the departments and centers at M.I.T. as well as persons associated with the Harvard Development Advisory Service and the Harvard Center for Population Studies," Dr. Levinson said.

The program's activities will include advisory services to governments and international agencies active in nutrition planning and programming, training programs for nutrition and planning personnel from low-income countries, and problem-oriented research on national and regional strategies to combat malnutrition, he said.

COMING NEXT ISSUE

- Chronic bronchitis
Accepted view as progressive, irreversible is challenged.
- Drug regulation
FDA head asks re-evaluation of thinking on methods.
- Decubitus ulcers
Application of hyperbaric oxygen may speed healing.

Wednesday, November 29, 1972

MEDICAL TRIBUNE

A Medical Tribune Alert: Upper Respiratory Infections

Amantadine May Curb Infection With Flu in Hospital Patients

ATLANTIC CITY, N.J.—"Routine amantadine prophylaxis in hospitalized patients" during outbreaks of influenza A has been recommended in addition to vaccination by a team of investigators from the University of Washington, Seattle.

Dr. J. Morgan O'Donoghue, Senior Fellow in the Department of Medicine, told the Interagency Conference on Antimicrobial Agents and Chemotherapy here that a 111-patient study undertaken last winter at Harborview Medical Center during a Seattle-area outbreak of influenza "showed that amantadine clearly prevented infection" in the hospital setting.

"Almost 20 percent of the patients who did not receive amantadine acquired nosocomial infection," he declared, "while among the amantadine-treated group only two patients had even serological evidence of infection."

Prophylactic amantadine, he maintained, "may result in significant physical and economic benefit to the chronically ill patient," who is more susceptible to severe complicating illnesses, such as pneumonia.

In the final week of December in 1971, Dr. O'Donoghue stated, influenza/Hong Kong/68 H₂N₂ strains were recovered from persons in the Seattle area. By the third week of January, a generalized influenza outbreak was under way in the community.

Influenza virus was isolated from a patient at the Harborview hospital during that week, and simultaneously, there was a sudden increase in staff absenteeism. Five of seven staff members tested showed serologic evidence of influenza infection.

Assigned on Number Basals

On February 1, and for the next 30 days, all patients admitted to the medical and neurologic services were assigned to amantadine treatment or non-treatment groups on the basis of odd or even hospital numbers.

Serologic tests were done both within 48 hours of admission and within one week after discharge. Some 60 patients were excluded from the study, Dr. O'Donoghue said, because of failure to obtain the discharge serology, or hospitalization for less than six days, or intra-hospital death.

The number of patients previously vaccinated was similar in both the amantadine and control groups, he observed, "but more important is the fact that the distribution of the initial hemagglutination-inhibition titers in the two groups was almost identical." Fifty per cent of both groups were deemed at great risk of acquiring influenza, with HI titers of 1:20 or less.

Of the seven patients who developed nosocomial influenza with clinical symptoms of malaise, myalgia, coryza, rhinitis, and fever more than 72 hours after admission, as well as virus isolation or fourfold antibody rise, none were receiving amantadine.

Of seven additional patients who had the fourfold antibody rise but remained free of clinical symptoms, only two were in the amantadine group.

Of those patients whose initial HI titers were 1:10 or less, six of 13 in the untreated group became infected, while only one in seven of the treated group did.

Five of the patients with clinical influenza, Dr. O'Donoghue pointed out, were hospitalized a total of 29 extra days solely as a consequence of their infection. "Two cases of severe influenza pneumonia occurred in patients with established reu-

matic heart disease and mitral stenosis and chronic obstructive pulmonary disease.

No complications of insomnia or hyperactivity or any organ toxicity were observed in the amantadine group, he remarked, at the dosage used, consisting of 100 mg. every 12 hours.

Beyond amantadine prophylaxis, Dr. O'Donoghue noted, the only other currently available means of preventing influenza infection is vaccination, "but this approach cannot protect a patient at the time of virus exposure."

Coauthors were Drs. Daniel Terry, C. George Ray, and Harry M. Beaty.

INFLUENZA INFECTION AMONG HOSPITALIZED PATIENTS

	Amantadine treated	Not treated
Clinical	0*/50	7*/61
Subclinical	2/50	5/61
Total	2**/50	12**/61

*p < 0.02 **p < 0.02 (X² analysis)

Microbiologist Throws Light on Flu Vaccine

MEDICAL TRIBUNE continues with its interview of Dr. Edwin T. Kilbourne.

Do you consider this line of research—recombination—the most promising for an eventual sure-fire influenza vaccine?

This is only one of several approaches using recombination. What this approach has done is to meet one specific need, and that is that it really helps us to leap the hurdle of strain mutation and production feasibility. The principle of recombination will always be useful no matter what kind of vaccine you have.

Other applications of this genetic manipulation of a virus involve the possibility of using a live virus vaccine, which brings with it the basic problem of achieving a certain critical level of attenuation so that the live virus does not cause disease but still immunizes. The advantages of using live virus vaccines are that they more closely simulate natural immunity, there is greater economy in that the virus can be diluted further than a dead virus, and they are easier to administer because they don't need to be injected.

How do you reply to the charges that the influenza vaccine simply doesn't work?

There certainly was a period when the production standards of the vaccine were not fully adequate, when undoubtedly vaccines of fairly low potency were distributed. However, a very carefully controlled study—and I have followed the field for more than 20 years—has shown that this is an effective vaccine. Another problem which may have created the lack of trust in the vaccine is the short-lived efficacy of the vaccine, the fact that it is not effective for longer than nine to 12 months. A further problem is the mutability of the virus and the fact that, as the virus antigenically drifts away from the strain of the vaccine, the vaccine becomes increasingly less effective. Thus, when we say that the vaccine is effective, it is with the caveat that you must use the proper strain and the proper dose, at the proper time. When these constraints are met, the vaccine is as effective as any vaccine we have, next to polio and smallpox.

One application of recombination having to do with ensuring that a live virus vaccine would not cause disease has been set forth by Dr. Robert Chanock, of the Laboratory of Infectious Diseases at the National Institute of Allergy and Infectious Diseases. He has had the ingenious idea of using temperature-sensitive mutants of a virus which multiply only in the upper respiratory tract and not in the lower, and, since most serious symptoms come from lower respiratory tract infections, this makes perfectly good sense. He has used the recombination mechanism to transfer this temperature-sensitive "defect" of one virus to another strain which is of the right antigenicity.

Lag Not Just Scientific

Currently, we still have a lag of at least three months before industry can supply the nation with the vaccine that antigenically matches the strain causing disease at the moment. This lag is occasioned more by administrative and economic problems than by the scientific problems of surveillance or of reaching a decision from isolation of strains from outbreaks around the world as to which is the prevalent strain.

In terms of avoiding this endless foot race with the virus in trying to keep up with the antigenic variations, I have a hypothesis that some of these new variants are the result of natural recombination with animal viruses. We could avoid this scurrying to keep up with changes in antigenicity by capturing these new antigens. In other words, if we were able to isolate and identify all of the present animal influenza A strains, we might obtain the strain that could cause the pandemic in 1978.

How do you regard the interferon approach?

I think that the principle of using a non-

a meaningful choice

Ser-Ap-Es[®] or

reserpine 0.1 mg
hydralazine hydrochloride 25 mg
hydrochlorothiazide 15 mg

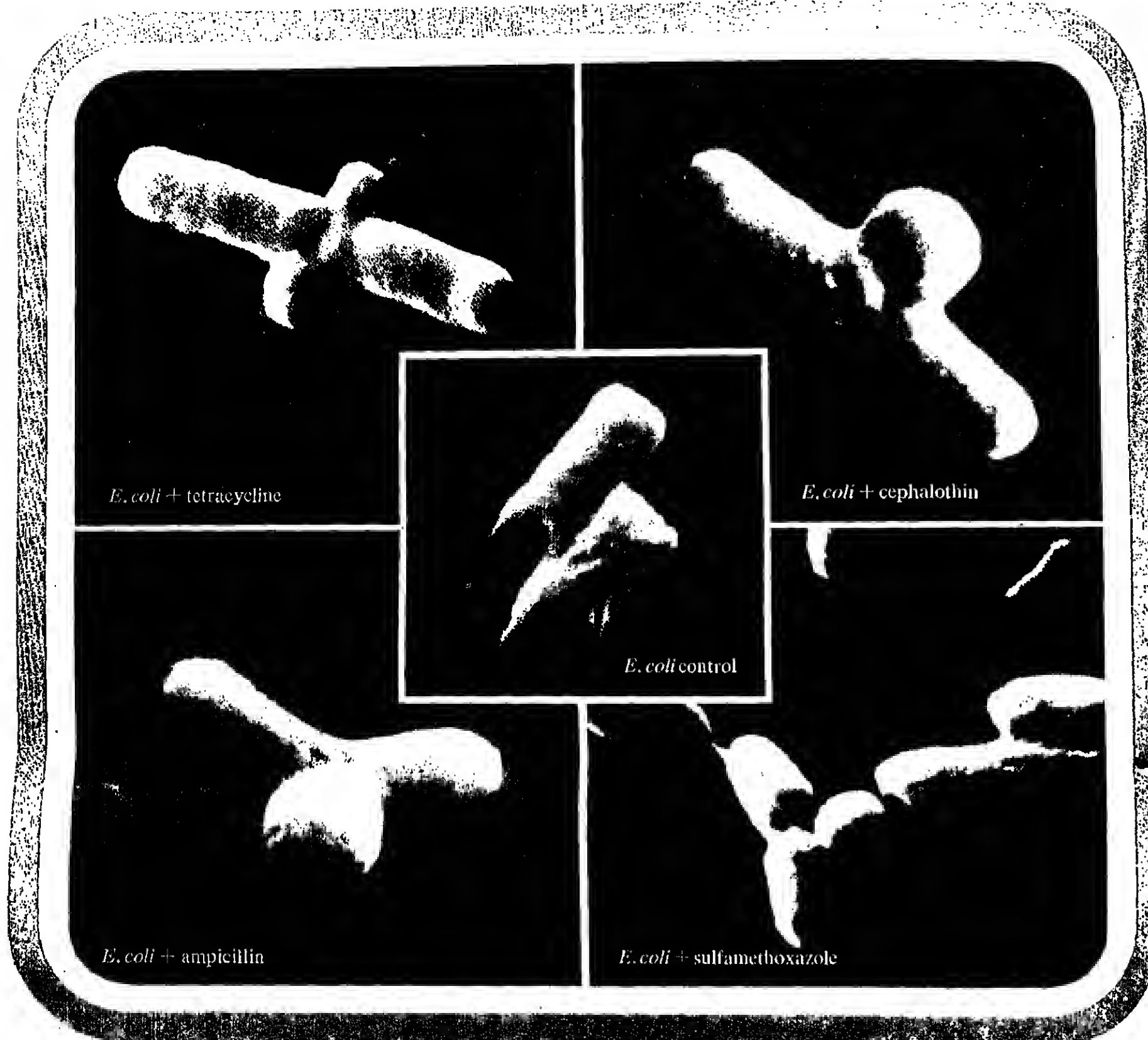
Esimil[®]

guanethidine monosulfate 10 mg
hydrochlorothiazide 25 mg

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Summit, New Jersey 07901

C I B A

Laboratory Research



Scanning Electron Microscope reveals changes in *E. coli* exposed to antibacterial agents

The Scanning Electron Microscope (SEM) is the only instrument which gives 3-dimensional views on a microscopic level. This permits the surface morphology of microorganisms to be observed in detailed perspective. Changes in surface morphology of *E. coli* exposed to various antimicrobial agents can be seen above.

Different mechanisms of antibacterial action—Similar changes in morphology

As part of a series of experiments,^{1,2} strains of *E. coli* proven susceptible to each antibacterial agent were exposed to 1 MIC of the respective antibacterials for a three-hour period. Included were cell-wall-active drugs, ampicillin and cephalothin; a drug interfering with intracellular protein synthesis, tetracycline; and a chemical agent which

acts by interference with para-aminobenzoic acid, sulfamethoxazole.

As seen above, elongation of the bacilli, midcell defects and spheroplast-like forms may be appreciated with the SEM technique. These changes in morphology were similar regardless of the antibacterial agent used and irrespective of its mechanism of action.

"At present, the significance of these observations in clinical infection must be considered with caution, but it is hoped that these data will stimulate a reevaluation of present concepts of the nature and role of morphological variants of bacteria exposed to a variety of antibacterial factors."²

It should be noted that no clinical conclusions can be drawn from this study, as it is not possible to extrapolate *in vitro* data to humans.

1. Klainer, A. S., Fass, R. J., and Perkins, R. L.: Scientific Exhibit presented at the 25th AMA Clinical Convention, New Orleans, La., Nov. 28-Dec. 1, 1971. 2. Klainer, A. S., and Perkins, R. L.: *Antimicrob. Agents Chemother.*, 1:164, 1972. 3. Klainer, A. S.: Data on file, Hoffmann-La Roche Inc., Nutley, N.J.

Clinical Practice

Control of primary bacterial offenders

Antibacterial Gantanol® (sulfamethoxazole) controls susceptible strains of *E. coli* and other gram-negative and gram-positive organisms often implicated in acute nonobstructed pyelonephritis and cystitis.

Prompt antibacterial blood and urine levels

In from 2 to 3 hours after the initial 2-Gm adult dose, antibacterial levels are present in both the blood and urine.

B.I.D./T.I.D. dosage schedules for around-the-clock coverage

Subsequent 1-Gm doses provide up to 12 hours of antibacterial coverage. More severe nonobstructed cystitis or pyelonephritis due to susceptible organisms may require a q. 8 h. dosage regimen. Either schedule provides coverage during the waking and sleeping hours—especially important during hours of sleep, when normal urinary retention tends to favor bacterial proliferation.

Also effective in nonobstructed chronic and recurrent u.t.i.

It is not uncommon for the elderly and debilitated to develop chronic and/or recurrent urinary tract infections such as pyelonephritis and cystitis. Gantanol (sulfamethoxazole) helps to bring these infections under control, when they are unaccompanied by obstruction and due to susceptible organisms. Frequent c.b.c.'s and urinalyses with microscopic examination are recommended.

Your option: Tablets or Suspension

Either dosage form—the Tablets or the pleasant-tasting, cherry-flavored Suspension—can provide the dependable antibacterial activity necessary to control nonobstructed cystitis or pyelonephritis. Symptomatic improvement may usually be expected in 24 to 48 hours. The usual precautions with sulfonamide therapy should be observed, including adequate fluid intake. Gantanol is generally well tolerated, with relative freedom from complications; the most common side effects are nausea, vomiting and diarrhea.

in nonobstructed cystitis or pyelonephritis due to susceptible organisms

Gantanol® (sulfamethoxazole) Basic Therapy

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Acute, recurrent or chronic nonobstructed urinary tract infections (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms. Note: Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response; add aminobenzoic acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of antibacterials including sulfonamides, especially in chronic or recurrent urinary tract infections. Measure sulfonamide blood levels as variations may occur; 20 mg/100 ml should be maximum total level.

Contraindications: Sulfonamide hypersensitivity; pregnancy at term and during nursing period; infants less than two months of age.

Warnings: Safety during pregnancy has not been established. Sulfonamides should not be used for group A beta-hemolytic streptococcal infections and will not eradicate or prevent sequelae (rheumatic fever, glomerulonephritis) of such infections. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy. Insufficient data on children under six with chronic renal disease.

Precautions: Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: Blood dyscrasias (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprotrombinemia and mel-

hemoglobinemia); allergic reactions (erythema multiforme, skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); gastrointestinal reactions (nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); CNS reactions (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); *musculoskeletal reactions* (drug fever, chills, toxic nephrosis with oliguria and anuria, periarthritis nodosa and L.E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuretics and hypoglycemia as well as thyroid malignancies in rats following long-term administration. Cross-sensitivity with these agents may exist.

Dosages: Systemic sulfonamides are contraindicated in infants under 2 months of age (except adjunctively with pyrimethamine in congenital toxoplasmosis).

Usual adult dosage: 2 Gm (4 tabs or teasp.) initially, then 1 Gm b.i.d. or t.i.d. depending on severity of infection.

Usual child's dosage: 0.5 Gm (1 tab or teasp.)/20 lbs of body weight initially, then 0.25 Gm/20 lbs b.i.d. Maximum dose should not exceed 75 mg/kg/24 hrs.

Supplied: Tablets, 0.5 Gm sulfamethoxazole; Suspension, 0.5 Gm sulfamethoxazole/teaspoonful.



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

SURGICAL NOTES

Child Kidney Transplants

SAN FRANCISCO—Children have excellent success with kidney transplants, according to investigators at the University of California Medical Center. They found that 80 per cent of an original 54 patients under 18 years of age had functioning grafts up to seven years after their operations, with a 20 per cent mortality.

While these results were felt to be encouraging, the investigators said that many problems remain to be solved in the care of children with end-stage renal disease.

Since most of the patients in the study received kidneys from relatives, the high success rate was anticipated. The success rate with cadaver donors, however, was slightly lower than the rate in adults, leading to the conclusion that testing for donor-recipient matching can be "much improved if not perfected."

Another question concerns the stage of kidney disease at which transplantation should take place, since children with chronic uremia grow poorly. Perhaps, the investigators suggested, these children should be considered for transplantation at a much earlier stage than usual, even before they require dialysis.

The investigators were Drs. Folkert O. Balzer, Robert T. Schwitzer, Malcolm Holliday, Donald Potter, and Samuel L. Kountz.

Wound Healing

KYOTO, JAPAN—A common misconception regarding reactions during wound healing is that a latent period exists for the first three days, a Finnish professor of forensic medicine said here, attributing the fallacy to dependence on studies by histologic techniques.

Today, with the use of enzyme histochemistry, dynamic changes can readily be detected in wounds as early as the first hour after injury, said Dr. J. Recknito, of the University of Turku.

Such information he noted, is of value not only to the forensic pathologist for the medicolegal estimation of the age of wounds, but also to the investigator who wishes to determine the toxicity of wound dressings.

Dr. Recknito addressed the fourth International Congress of Histochemistry and Cytochemistry.

Success in Liver Grafts

ATHENS—Continued study of the problems of liver grafting is being rewarded by some successes, Dr. Roy Calne, of Addenbrooke's Hospital, Cambridge, England, said at the eighth Panhellenic Congress of Surgery.

"In the Cambridge-Kings College Hospital series," he said, "the longest survivor after orthotopic liver grafting is in excellent health three and a half years following the transplant operation."

"Better results from liver transplants will be obtained when patients are treated before they are moribund and when there are better methods of conserving the liver."

Acupuncture in Animals

PEKING—Chinese veterinary surgeons have proved during the last two years that acupuncture anesthesia works just as well on animals as on human beings, China's Hsinhua News Agency reported.

The trials were conducted with 360 horses and with other animals by a joint team from the Peking Municipal Veterinary Hospital and the Peking Horse Disease Prevention and Treatment Center of the People's Liberation Army.

The investigators reported a 95 per cent success rate, and commented:

"The fact that so many horses, mules, donkeys, cattle, and pigs have responded to the method should be an eloquent denial of some skeptics' reasoning that success with human beings has been due to psychological indoctrination."

Evaluation of 5 sleep medications in the sleep research laboratory^{1,2}

A CLEAR DEMONSTRATION OF DALMANE[®] EFFECTIVENESS (flurazepam HCl)

Patients fell asleep faster

Average number of minutes required to fall asleep

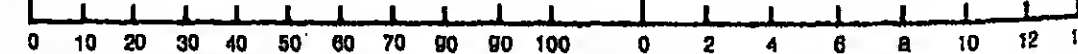
DALMANE
(flurazepam HCl)
(30 mg)
3 placebo baseline nights
First 3 medication nights
13-14th medication nights

Chloral hydrate
(1000 mg)
3 placebo baseline nights
First 3 medication nights
13-14th medication nights

Glutehimide
(500 mg)
3 placebo baseline nights
First 3 medication nights
13-14th medication nights

Methaqualone
(300 mg)
3 placebo baseline nights
First 3 medication nights
13-14th medication nights

Secobarbital
(100 mg)
3 placebo baseline nights
First 3 medication nights
13-14th medication nights



References:

1. Keles, A.: "The Evaluation and Treatment of Insomnia," Scientific Exhibit presented at Clinical Convention, A.M.A., New Orleans, La., Nov. 28-Dec. 1, 1971.
2. Keles, A., et al.: Arch. Gen. Psychiat., 23:226, 1970.

...had less trouble staying asleep

Average number of awakenings after the onset of sleep

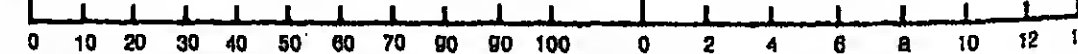
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(300 mg)
3 placebo baseline nights
First 3 medication nights
13-14th medication nights

Secobarbital
(100 mg)
3 placebo baseline nights
First 3 medication nights
13-14th medication nights



...and slept longer

Percentage of time spent sleeping

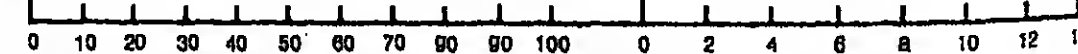
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(300 mg)
3 placebo baseline nights
First 3 medication nights
13-14th medication nights

Secobarbital
(100 mg)
3 placebo baseline nights
First 3 medication nights
13-14th medication nights



Sleep research laboratory studies confirm the effectiveness of **DALMANE**[®] (flurazepam HCl) when restful sleep is indicated

One 30-mg capsule h.s.—usual adult dosage.
One 15-mg capsule h.s.—initial dosage for elderly or debilitated patients.



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■ On average induced sleep within 17 minutes and decreased nocturnal awakenings.

■ Morning "hang-over" has been relatively infrequent. Dizziness, drowsiness, lightheadedness and the like were the side effects noted most frequently, particularly in elderly or debilitated patients.

■ One 30-mg capsule at bedtime provided 7 to 8 hours of sleep without need to repeat or increase dosage.

Before prescribing Dalmane (flurazepam HCl), please consult Complete Product Information, a summary of which follows:
Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakenings. In patients with recurring insomnia or poor sleeping habits; and in acute or chronic medical situations requiring restful sleep. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended.

Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 18

years of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude overdosage, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe reactions, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported.

Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pain, body and joint pains and GU complaints. There have also been rare occurrences of sweating, flushing, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations and elevated SGOT, SGPT, total and direct bilirubin and alkaline phosphatase. Paradoxical reactions, e.g., excitement, stimulation and hyperactivity, have also been reported in rare instances.

Dosage: Individualize for maximum beneficial effect. Adults: 30 mg usual dosage; 15 mg may suffice in some patients. Elderly or debilitated patients: 15 mg initially until response is determined.

Supplied: Capsules containing 15 mg or 30 mg flurazepam HCl.

Objectively demonstrated

by 5 sleep research laboratory studies

How effective are sleep medications in inducing sleep, decreasing nighttime awakenings and improving total sleep time? These questions have been answered clearly and objectively by sleep research laboratories.

Data shown here derive from 5 such studies of 5 sleep medications undertaken by a leading sleep research investigator.

Initially all agents were moderately to markedly effective in at least one of the parameters measured, while Dalmane was consistently effective in all parameters. In addition, the author noted, at the end of two weeks' administration, tolerance had developed to all drugs except Dalmane (flurazepam HCl).

22-Night Protocol Design and Reasons for Design

Night	Placebo	Drug	Lab	Reason for Design
1		X		Adaptation to environment
2 to 4	X	X		Baseline measurements
5 to 7		X	X	Initial and short-term drug effects
8 to 15		X	X	Evaluation in home surroundings
16		X	X	Readaptation to laboratory
17 & 18	X	X		Long-term (14 nights) drug effectiveness
19 to 22	X	X		Evaluation of withdrawal effects

* Data appearing in the graphs to the left

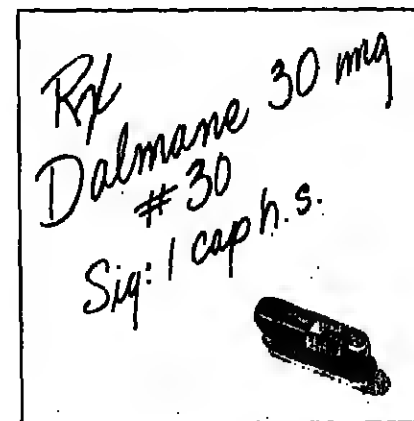
Subjectively confirmed by patient reports

Every morning, patients described the previous night's sleep. These subjective reports, the author noted, were in agreement with the objective EEG data and indicated that Dalmane provided definite improvement in sleep responses.

While no adverse clinical reactions with Dalmane were reported in these studies, dizziness, drowsiness, lightheadedness and the like have been noted, particularly in the elderly or debilitated. (An initial dose of Dalmane 15 mg should be prescribed for these patients.)

DALMANE[®]
(flurazepam HCl)

when restful sleep is indicated



Arterial Disease In Diabetes Said To Require Study

Medical Tribune World Service

STOCKHOLM—"The mysterious statement that diabetes enhances the development of atherosclerosis is repeated over and over again in all respectable textbooks, but in my opinion this is one of the greatest stumbling blocks for the advancement of macroangiopathy research," a Danish physician declared here.

Speaking on diabetes and the heart at a Skandia International Symposium on early phases of coronary heart disease, Dr. Knud Lundbaek suggested that there is need for re-evaluation of the entire problem of diabetic large-vessel disease and, in particular, coronary vessel disease.

Dr. Lundbaek, who is with the University Department of Medicine M, Municipal Hospital, Aarhus, Denmark, suggested the following as a working hypothesis:

"The abnormalities of the large external branches of the coronary artery in long-term diabetics are a mixture of atherosclerosis and some kind of medial sclerosis, perhaps more atherosclerosis in old subjects, perhaps more medial sclerosis in young ones."

Proposes Usable Hypothesis

He cited the need for quantitative studies of the relationship between the macroangiopathy of the extramural vessels and the microangiopathy of the myocardial network. As a hypothesis that might be used for a combined clinical and histologic study, he proposed:

"The high incidence of coronary infarction and the high primary mortality in diabetics is due to the fact that these patients have two or three vascular abnormalities—diabetic microangiopathy, diabetic macroangiopathy, and, usually atherosclerosis."

Considering the "enormous number" of morphologic studies of microangiopathy in the eyes, kidneys, brain, skin, muscle, and gastrointestinal tract, Dr. Lundbaek described it as surprising that only a handful of papers deal with the intramural branches and capillaries in the coronary system. He also observed that diabetic macroangiopathy has not attracted much attention.

Dr. Lundbaek said that medial sclerosis with intimal calcification of diabetic patients has never been studied histologically, either qualitatively or quantitatively, nor have there been large-scale studies of the relationship between medial sclerosis and duration of diabetes.

"From my own experience and that of my co-workers," he commented, "it is rather certain that, in young patients, medial sclerosis occurs only after many years of diabetes, but much more work has to be done to see if this relationship is as characteristic as the relationship between microangiopathy and duration of diabetes, and if, in the individual patients, microangiopathy and medial sclerosis develop in a parallel fashion," he said.

Dr. Lundbaek said that he and his co-workers have suggested that hypersecretion of growth hormone may be a causal factor in the development of diabetic microangiopathy.

Investigators to Develop Pathophysiology Material

BALTIMORE—A two-year project to develop educational resource material for teaching the gastrointestinal and liver-related portions of medical school courses in pathophysiology will be directed by Dr. Theodore M. Bayless, Associate Professor of Medicine, Johns Hopkins University School of Medicine.

Dr. Bayless will coordinate the work of a number of subgroups of investigators and teachers at several medical schools. The project is being supported by a grant from the National Fund for Medical Education to the American Gastroenterological Association.



It may be just a mild depression. But she needs help...and needs it right now. Counsel and reassurance may suffice. But if you decide supportive medication is indicated, Ritalin can

offer prompt benefit. No need to wait days or weeks to begin feeling better. Ritalin improves mood and outlook, helps the patient get moving again.

Ritalin is generally well tolerated, even by older or convalescent patients. And there's generally no need for long-term therapy. When Ritalin works, one prescription may be sufficient.

Ritalin[®] (methylphenidate) helps overcome the inertia of mild depression*

*This drug has been evaluated as possibly effective for this indication. See brief summary.

Ritalin[®] hydrochloride
(methylphenidate hydrochloride)
TABLETS

INDICATION
Based on a review of this drug by the National Academy of Sciences-National Research Council and for other information, FDA has classified the indication as follows:
"Possibly" effective: Mild depression
Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS
Marked anxiety, tension, and agitation, since Ritalin may aggravate these symptoms. Also contraindicated in patients known to be hypersensitive to the drug and in patients with glaucoma.

WARNINGS
Ritalin is not recommended for children under six years, since safety and efficacy in this age group have not been established. Since sufficient data on safety and efficacy of long-term use of Ritalin in children with minimal brain dysfunction are not yet available, those requiring long-term therapy should be carefully monitored. Ritalin should not be used for severe depression or other exogenous or endogenous origin or for the prevention of normal fatigue states.

Ritalin may lower the convulsive threshold in patients with or without prior seizures; with or without prior EEG abnormalities, even in absence of seizures. Safe concomitant use of anticonvulsants and Ritalin has not been established. If seizures occur, Ritalin should be discontinued.

Drug Interactions
Ritalin may decrease the hypotensive effect of guanethidine. Use cautiously with pressor agents and MAO inhibitors. Ritalin may inhibit the metabolism of coumarin anticoagulants, anticonvulsants (phenobarbital, diphenylhydantoin, primidone), phenylbutazone, and tricyclic antidepressants (imipramine, desipramine). Downward dosage adjustments of these drugs may be required when given concomitantly with Ritalin.

Usage in Pregnancy
Adequate animal reproduction studies to establish safe use of Ritalin during pregnancy have not been conducted. Therefore, until more information is available, Ritalin should not be prescribed for women of childbearing age unless, in the opinion of the physician, the potential benefits outweigh the possible risks.

Drug Dependence
Ritalin should be given cautiously to emotionally unstable patients, such as those with a history of drug dependence or alcoholism, because such patients may increase dosage on their own initiative.

Chronicity of abuse can lead to marked tolerance and psychic dependence with varying degrees of abnormal behavior. Frank psychotic episodes can occur, especially with parenteral abuse. Careful supervision is required during drug withdrawal, since severe depression as well as the effects of chronic overactivity can be unmasked. Long-term follow-up may be required because of the patient's basic personality disturbances.

PRECAUTIONS
Patients with an element of agitation may react adversely to discontinuation of therapy if necessary. Periodic CBC and platelet counts are advised during prolonged therapy.

ADVERSE REACTIONS
Nervousness and insomnia are the most common adverse reactions but are usually controlled by reducing dosage and omitting the drug in the afternoon or evening. Other reactions include: hypersensitivity (including skin rash, urticaria, fever, erythema, exfoliative dermatitis, and erythema multiforme with histopathological findings of necrotizing vasculitis); anorexia; nausea; dizziness; palpitations; headache; dyskinetic; drowsiness; blood pressure and pulse changes, both up and down; tachycardia; angina; cardiac arrhythmias; abdominal pain; weight loss during prolonged therapy; in children, loss of appetite, abdominal pain, weight loss during prolonged therapy, insomnia, and tachycardia may occur more frequently. Toxic psychosis has been reported.

DOSEAGE AND ADMINISTRATION
Adults: Administer orally in divided doses 2 or 3 times daily, preferably 30 to 45 minutes before meals. Dosage will depend upon indication and individual response. Average dosage is 10 to 30 mg daily. Some patients may require 40 to 60 mg daily. In others, 10 to 15 mg daily will be adequate. The few patients who are unable to sleep at night should take the last dose before 6 p.m.

HOW SUPPLIED
Tablets, 20 mg (pink, scored); bottles of 100 and 1000.
Tablets, 10 mg (pink, scored); bottles of 100, 500, 1000 and 5000.
Tablets, 5 mg (pink, scored); bottles of 100, 500, and 1000.

Consult complete product literature before prescribing.

CIBA Pharmaceutical Company
Division of CIBA-GEIGY Corporation
Summit, New Jersey 07901

C I B A

Wednesday, November 29, 1972

MEDICAL TRIBUNE

11

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Clinical Trials and Mistrials—a Postscript

THE DEFINITION of a camel as a horse designed by a committee aptly describes the clinical trial. Ungainly, cumbersome, and plodding, it is nonetheless an essential vehicle for research that reaches its objective if properly directed. Or, as happens all too often, it can stray aimlessly in an arid wasteland of statistical data. Many have thought that this is just what happened in the University Group Diabetes Program trial of hypoglycemic agents and have voiced criticisms of the U.G.D.P. study's design, analysis, and conclusions. To resolve the controversy, which has continued for over two years (since the findings were first released in unorthodox manner in 1970), the director of the National Institutes of Health, Dr. Robert O. Merston, has invited an ad hoc international jury of seven biometricians of the Biometric Society to conduct a post hoc trial of the trial. Its object will be to decide whether the study is meritorious or meretricious, whether it is a sow's ear or silk purse. We hope that among the biometricians there are some who are also able clinicians.

And, speaking of purses, the clinical trial is a costly as well as complex type of clinical investigation. One division of the NIH alone, the National Heart and Lung

Institute, is expending some \$130,000,000 over the next decade in clinical trials relating principally to coronary heart disease prevention and therapy.

A short fable of Ambrose Bierce titled "The Flying Machine" appears pertinent to the pitfalls and pitfalls of some clinical trials. "An Ingenious Man who had built a flying machine invited a great concourse of people to see it go up. At the appointed moment, everything being ready, he boarded the car and turned on the power. The machine immediately broke through the massive substructure upon which it was built, and sank out of sight into the earth. The aeronaut springing out berily in time to save himself, 'Well,' said he, 'I have done enough to demonstrate the correctness of my details. The defects,' he added, with a look in the ruined brick work, 'are merely basic and fundamental.' On this assurance the people came forward with subscriptions to build a second machine."

As a postscript it should be noted that *Fantastic Fables* was published in 1899. A flying machine built in 1903 by the Wright Brothers was more successful, proving that an experiment designed well and executed without fanfare may very well work.

R.S.G.

For the Birds

FEEDING BIRDS from what *New Scientist* calls a "bird table" on an urban back porch is fraught with problems, as anyone who does it knows.

The squirrels, of course, are the primary problem, since they are able to inhale the contents of a feeder in eight seconds while hanging upside down in space. An old 12-inch record (the "Nutcracker Suite," by some ridiculous chance), suspended over a hanging feeder, keeps our squirrels from approaching from above; and cantilevering the feeder sufficiently far out into space keeps them from flying through the air to it. It also makes filling the thing one of the more dangerous acrobatic acts in the neighborhood and has sent the frustrated squirrels raging through the backyard ripping off half the living things there.

The pigeons were defeated by the same means that rid us of squirrels (they can't perch on the hanging feeder), but we lost the nonperching mourning doves too. And why, if it comes to that, do we hate pigeons and love mourning doves?

Then there are the stray cats sitting on the porch in the early mornings waiting for

the birds to come so everyone can an. (The cats seem to have worked out a non-aggression pact with the squirrels, whom they never bother.) The last dog we had kept away cats, it's true, but he also kept away birds. There's no simple victory.

These reflections were prompted by a piece in *New Scientist* by the current president of the Botanical Society of the British Isles, who is less interested in getting the seeds into the birds than in what the seeds are that are present in commercial mixes and what happens to them when they fall onto the ground and germinate. This botanical question may not be of overwhelming interest to everyone, but what caught us was a table listing the "jargon" names of the seeds in various mixes—blue maw, mazagan canary, gold of pleasure, black rape, French teazle, among others. Nice names.

And what scared us a little was to find hemp also named, old Cannabis sativa itself, on the list of botanic names. Looks as if we're going to have to police the area to see what's germinating before the law breaks in with axes.

D.S.

On Treating Hypertension

CLINICAL QUOTE: "It has now been shown beyond a reasonable doubt that specific treatment with specific antihypertensive medication is not only effective in preventing or greatly reducing mortality due to the disease but is also quite effective in reducing morbidity resulting from hypertension and its complications.

Consequently, it is timely that a major effort should be made to identify and treat patients with hypertensive disease." (Dr. John H. Moyer, Professor of Medicine, Hahnemann Medical College and Hospital, commenting on the National Heart and Lung Institute nationwide campaign against hypertension; see page 1.)



"After all, Hippocrates isn't the only fish in the sea. Why not get another opinion?"

LETTERS TO THE EDITOR

Cesareans by Whom?

Editor, MEDICAL TRIBUNE:

I see no need to train family practice residents in doing cesarean sections as Dr. Kermit Krantz, of the Department of Obstetrics, University of Kansas, suggests (October 25). I doubt that Dr. Krantz can name many first-class hospitals which allow board-certified family practitioners cesarean section privileges. I firmly believe the family practitioner should give obstetrical care, including vaginal delivery, and the main feature of his training should be the management of all types of vaginal deliveries, obstetrical complications, and the ability to recognize the need for cesarean section and where to find consultative and referral help when needed.

I think the main problem facing the American Academy of Family Practice is a clear definition of what family practice includes. It does not in my opinion include any type of general surgery, and in view of the restrictiveness of most hospital staffs, I do not feel the residents' training should be wasted in these fields.

ALBERT L. GNASICK, M.D. A.B.F.P.
New Oxford, Pa.

Congressman Rogers

Editor, MEDICAL TRIBUNE:

Congratulations for Dr. Sackler's wonderful editorial about Congressman Paul Rogers. I met him twice in my life and can only confirm what Dr. Sackler said in his column.

Congressman Rogers really deserves the honorary degree of Doctor of Humane Letters and MEDICAL TRIBUNE's Award of Merit. A wonderful man—if he should run for Presidency of the United States, he should have my vote immediately.

DR. HENRY M. STRATTON
President,
Intercontinental Medical Book Corp.
New York, N.Y.

Abortion Anatomized

Editor, MEDICAL TRIBUNE:

It was with an intense feeling of nausea and disgust that I read your news article entitled "Induction of Abortion: Saline and Prostaglandin Compared" (September 13).

To what depths has the medical profession descended, and to what barbaric heights have we regressed, when a respectable medical publication can report as a bona fide scientific, therapeutic service a deliberately death-dealing procedure such as this? (Shades of the Nazi tyranny!)

This has to be an all-time low in medical journalism. And any institution allowing the carrying on of such research into more efficient methods of killing innocent human beings deserves no place in medical education.

If it were not for mere curiosity as to what more can develop to lessen our respect for human life, I should ask that my name be scratched from your mailing list.

I am sure I voice the sentiments of literally hundreds, if not thousands, of conscientious physicians who are horrified at the insensate slaughter of innocent babies in New York and elsewhere in the so-called more enlightened states in which legal "therapeutic" abortion is permitted.

WALLACE W. MCWHIRTER, M.D.
Tucson, Ariz.

Focus on Hypertension

Editor, MEDICAL TRIBUNE:

I am delighted with the coverage you have given to the National Heart and Lung Institute's campaign on hypertension.

It has been comprehensive in scope and very helpful to the national campaign.

THEODORE COOPER, M.D.
Director,
National Heart and Lung Institute

Thanks to Us

Editor, MEDICAL TRIBUNE:

I want to thank you for MEDICAL TRIBUNE. I must commend you particularly on the accuracy of your reporting.

OSCAR D. RATNOFF, M.D.
Case Western Reserve University
Cleveland, Ohio

Consent: What's Proper?

Editor, MEDICAL TRIBUNE:

Regarding your report, "Breast Surgery: Proper Consent Under Debate," October 11. In many jurisdictions there are legal rulings that authoritative medical articles and texts may be introduced in malpractice suits as evidence.

There is no absolute in what you should tell a patient, any more than there is an absolute guarantee in the practice of medicine. For example: I had a patient with an early melanoma and referred her to a good surgeon. He advised wide local excision. She got another opinion from an equally good surgeon that the lymph glands should be dissected. That done, she was forced to make the decision herself, through her choice of surgeon.

ALEX D. CAMPBELL, M.D.
Bellevue, Wash.

Medical Tribune

November 29, 1972

The three different effects of Valium® (diazepam)

psychotherapeutic anticonvulsant skeletal muscle relaxant

Since the introduction of Valium (diazepam) in 1963, worldwide clinical experience has confirmed its effectiveness in relieving excessive psychic tension. Extensive clinical trials—supported by highly sophisticated laboratory and pharmacologic studies—have established its value in several other important areas of medicine. To date, some 7,000 scientific reports in the world literature have contributed to the body of knowledge about Valium.

The following overview—a reflection of extensive clinical experience—describes how Valium can be beneficial as a psychotherapeutic agent, anticonvulsant and skeletal muscle relaxant, and how it is recommended to be used in office and hospital practice, in the oral and injectable forms.

Please see the last page of this advertisement
for complete prescribing information.

This advertisement is printed on recycled paper.



500-1111

The psychotherapeutic effect of Oral Valium® (diazepam)

in anxiety and somatic symptoms of excessive psychic tension

When a complete examination rules out organic disease, you may find that functional complaints involving the heart, stomach or colon—frequently seen in anxious patients overreacting to stress—are a result of excessive psychic tension. And if counseling alone does not suffice, you might consider Valium (diazepam) to help relieve these tension-induced symptoms. In general, it goes to work promptly,

usually producing significant improvement within the first few days of therapy, although some patients may take longer to show a clear-cut response.

Available in three convenient tablet strengths—2 mg, 5 mg, 10 mg—Valium provides dosage flexibility for maximum patient benefit with a typical *t.i.d.* or *q.i.d.* regimen.



in anxiety with or without associated depressive symptoms in psychoneurotics

Valium (diazepam) can provide prompt relief when excessive anxiety and undue tension are a prominent part of the clinical picture. By relieving these symptoms, it can enhance response to therapy and add to the effectiveness of your total management of the psychoneurotic patient. Caution patients against driving or engaging in hazardous activities during therapy.

The recommended dosage is 2 to 10 mg, *b.i.d.* to *q.i.d.*, depending upon the severity of symptoms.

adjunctively in organic disorders complicated by undue psychic tension

Overly tense patients—particularly those with C.I. or cardiac disease—must be kept calm when undue tension and excessive anxiety aggravate their condition and interfere with therapy. Oral Valium can provide the desired response, generally without significantly adversely affecting respiratory, pulse or heart rates. It is used with most classes of primary medications such as cardiac glycosides, diuretics, vasodilators, anticholinergics and antacids, and is usually well tolerated; the most frequent side effects are drowsiness, fatigue and ataxia.

When nighttime anxiety precludes sleep, an *h.s.* dose added to the *t.i.d.* regimen can relieve the anxiety.



Please see the last page of this advertisement for complete prescribing information.

The psychotherapeutic effect of Injectable Valium® (diazepam)

prior to surgery

Injectable Valium (diazepam) can promptly calm the surgical patient by lessening the excessive anxiety and undue tension that may be associated with strange surroundings and disturbing procedures. And it can provide the added advantage of markedly diminishing recall of preoperative procedures.

The recommended dosage is 10 mg, I.M., administered one to two hours preoperatively. Injectable Valium should not be mixed or diluted with other drugs, solutions or fluids.

adjunctively prior to gastroscopy and esophagoscopy

Injectable Valium (diazepam) can be a valuable adjunct in allaying excessive anxiety when it accompanies such procedures. It calms the anxiety yet allows the patient to cooperate by responding to commands and following instructions. It is not recommended for bronchoscopy and laryngoscopy. Because of the possibility of laryngospasm, necessary countermeasures and resuscitative facilities should be immediately available.

Half an hour before gastroscopy or esophagoscopy, a 5 to 10-mg dose is administered I.M. or I.V.



prior to cardioversion

Through relief of undue anxiety and excessive tension, Injectable Valium (diazepam) can effectively calm the patient. Memory of the cardioversion procedure can be markedly diminished. Injectable Valium seldom significantly alters vital signs. Nevertheless, there have been infrequent reports of hypotension and rare reports of apnea and cardiac arrest. Resuscitative facilities should be immediately available.

Five to ten minutes before elective cardioversion, the recommended dosage is 5 to 15 mg, injected slowly I.V. (5 mg/min).



The anticonvulsant effect of Valium® (diazepam)

adjunctively in certain convulsive disorders

Injectable Valium (diazepam) has usually been an effective adjunct in interrupting status epilepticus promptly, sometimes in a matter of seconds. It has helped provide control with the first injection, frequently with prolonged relief. Oral Valium may be used adjunctively in certain convulsive disorders such as petit mal or myoclonic seizures, although it has not proved useful as sole therapy.

In status epilepticus and severe recurrent convulsive seizures, 5 to 10 mg, injected slowly I.V.—5 mg (1 ml)/minute. Use I.M. route if slow I.V. injection is not feasible. Do not mix or dilute with other drugs, solutions or fluids. Repeat in 2 to 4 hours, if necessary. The dosage for Oral Valium used adjunctively is 2 to 10 mg, 3 or 4 times a day.



Please see the last page of this advertisement for complete prescribing information.

The skeletal muscle relaxant effect of Valium® (diazepam)

adjunctively in skeletal muscle spasm caused by local pathology

As part of the therapeutic regimen, Valium (diazepam) orally or parenterally, as appropriate, can help relieve skeletal muscle spasm due to reflex spasm caused by local pathology, such as inflammation of muscles or joints, or associated with muscle strains. It can help break the spasm/pain/spasm cycle and thus may increase mobility. Usual oral dosage is 2 to 10 mg on a *t.i.d.* or *q.i.d.* schedule.

Usual injectable dosage is 5 to 10 mg I.M. or I.V. initially, then 5 to 10 mg in 3 to 4 hours, if necessary. In elderly or debilitated patients, it is recommended that oral dosage be limited to the smallest effective amount to preclude the development of ataxia or oversedation (2 to 2½ mg once or twice daily, initially, to be increased gradually as needed and tolerated).



adjunctively in spasticity due to cerebral palsy or athetosis

The skeletal muscle relaxant effect of Valium (diazepam) makes it a valuable adjunct in reducing spasticity. It may thus aid by reducing involuntary movements and improving voluntary performance and speech. This may result in more patient cooperation and confidence during therapy. Valium is generally well tolerated; drowsiness has been the biggest problem among responsive athetoid children. The possible side effect of ataxia may limit its usefulness in ataxic children.

Dosage should be individualized for maximum patient benefit. However, the usual recommendation is 2 to 10 mg *t.i.d.* or *q.i.d.* Where parenteral therapy is indicated, use 5 to 10 mg I.M. or I.V. initially, then 5 to 10 mg in 3 to 4 hours, if necessary. Oral Valium is contraindicated in children under 6 months and Injectable Valium is contraindicated in infants.

adjunctively in spasticity associated with paraplegia

In upper motor neuron disorders causing paraplegia, the adjunctive use of Valium (diazepam) can help reduce skeletal muscle spasticity. Valium offers a wide margin of safety due to its relatively low toxicity. Isolated reports of neutropenia and jaundice make periodic blood counts and liver function tests advisable during long-term therapy.

Three convenient tablet strengths—2 mg, 5 mg, 10 mg—allow wide adjustments in dosage for the greatest efficacy in clinical response. And Injectable Valium may be used, where appropriate, in the usual dosage for muscle spasm.

parenterally in stiff-man syndrome or in tetanus

Injectable Valium (diazepam), used adjunctively, can reduce characteristic skeletal muscle spasm and resulting rigidity. Response is usually prompt, and improvement sustained in the control of muscular rigidity and convulsive spasms. In general, Valium can thus help improve range of mobility. Periodic blood counts and liver function tests are advisable during long-term therapy. Only the parenteral form of Valium (diazepam) is indicated for tetanus. Usual I.M. or I.V. dosage recommendation is 5 to 10 mg; for tetanus, larger doses may be required. A repeat dose, if necessary, may be administered in 3 to 4 hours.

For three different effects:
psychotherapeutic
anticonvulsant
skeletal muscle relaxant

Valium®
(diazepam) 

Please see the following page for complete prescribing information.

Valium® (diazepam)

2-mg, 5-mg, 10-mg tablets

ready-to-use 2-ml Tel-E-Ject™ (disposable syringes)

10-ml vials } 5 mg/ml
2-ml ampuls }

Complete Prescribing Information:

Description (ORAL AND INJECTABLE): Valium (diazepam) is a benzodiazepine derivative developed through original Roche research. Chemically, diazepam is 7-chloro-1-methyl-5-phenyl-2H-1,4-benzodiazepin-2-one. It is a colorless, crystalline compound, insoluble in water and has a molecular weight of 284.74.

Pharmacology (ORAL AND INJECTABLE): In animals Valium (diazepam) appears to act on parts of the limbic system, the thalamus and hypothalamus, and induces calming effects. Valium (diazepam), unlike chlorpromazine and meprobamate, has no demonstrable peripheral autonomic blocking action, nor does it produce extrapyramidal side effects; however, animals treated with Valium (diazepam) do have a transient ataxia at higher doses. Valium (diazepam) was found to have transient cardiovascular depressor effects in dogs. Long-term experiments in rats revealed no disturbances of endocrine function. Injections into animals have produced localized irritation of tissue surrounding injection sites and some thickening of veins after intravenous use.

Oral LD₅₀ of diazepam is 720 mg/kg in mice and 1540 mg/kg in rats. Intraperitoneal administration of 400 mg/kg to a monkey resulted in death on the sixth day.

Reproduction Studies: A series of rat reproduction studies was performed with diazepam in oral doses of 1, 10, 80 and 100 mg/kg. At 100 mg/kg there was a decrease in the number of pregnancies and surviving offspring in three rats. Neonatal survival of rats at doses lower than 100 mg/kg was within normal limits. Several neonates in these rat reproduction studies showed skeletal or other defects. Further studies in rats at doses up to and including 80 mg/kg/day did not reveal teratological effects on the offspring.

In humans, measurable blood levels of Valium (diazepam) were obtained in maternal and cord blood, indicating placental transfer of the drug.

Indications:

ORAL AND INJECTABLE:

Valium (diazepam) is useful in the symptomatic relief of tension and anxiety states resulting from stressful circumstances or whenever somatic complaints are concomitants of emotional factors. It is useful in psychomotor states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation.

In acute alcohol withdrawal, Valium (diazepam) may be useful in the symptomatic relief of acute agitation, tremor, impending or acute delirium tremens and hallucinations. Valium (diazepam) is a useful adjunct for the relief of skeletal muscle spasm due to reflex spasm to local pathology (such as inflammation of the muscles or joints, or secondary to trauma); spasmically caused by upper motor neuron disorders (such as cerebral palsy and paraplegia); atetosis; stiff-man syndrome.

ORAL: Oral Valium (diazepam) may be used adjunctively in convulsive disorders, although it has not proved useful as the sole therapy.

Injectable: If apprehension, anxiety and acute stress reactions are present prior to gastroscopy and esophagoscopy, injectable Valium (diazepam) may be a valuable adjunct. (See Precautions.)

Injectable Valium (diazepam) is a useful adjunct in status epilepticus and severe recurrent convulsive seizures, and in tetanus.

Valium (diazepam) is a useful premedication (the I.M. route is preferred) for relief of anxiety and tension in patients who are to undergo surgical procedures. Intravenously, it is also useful prior to endotracheal intubation. In either instance, the patient's recall of the procedure is markedly diminished.

Contraindications:

ORAL: Valium (diazepam) is contraindicated in patients with a known hypersensitivity to this drug and, because of lack of sufficient clinical experience, in children under 6 months of age. It may be used in patients with open angle glaucoma who are receiving appropriate therapy, but is contraindicated in acute narrow angle glaucoma.

Injectable: Injectable Valium (diazepam) is contraindicated in infants and in patients with a known hypersensitivity to this drug. It may be used in patients with open angle glaucoma who are receiving appropriate therapy, but is contraindicated in acute narrow angle glaucoma.

Warnings:

ORAL AND INJECTABLE: As is true of most CNS-acting drugs, patients receiving Valium (diazepam) should be cautioned against engaging in hazardous occupations requiring complete mental alertness, such as operating machinery or driving a motor vehicle.

Since Valium (diazepam) has a central nervous system depressant effect, patients should be advised against the simultaneous ingestion of alcohol and other CNS-depressant drugs during Valium (diazepam) therapy.

ORAL: Valium (diazepam) is not of value in the treatment of psychotic patients and should not be employed in lieu of appropriate treatment.

As with other agents which have anticonvulsant activity, when Valium (diazepam) is used as an adjunct in treating convulsive disorders, the possibility of an increase in the frequency and/or severity of grand mal seizures may require an increase in the dosage of standard anticonvulsant medication. Abrupt withdrawal of Valium (diazepam) in such cases may also be associated with a temporary increase in the frequency and/or severity of seizures.

Injectable: When used intravenously the solution should be injected slowly, directly into the vein, taking at least one minute for each 5 mg (1 ml) given. Do not mix or dilute injectable Valium (diazepam) with other solutions or drugs. Do not add to I.V. fluids. Rare reports of apnea or cardiac arrest have been noted, usually following I.V. administration, especially in elderly or very ill patients and those with limited pulmonary reserve. Duration is generally brief. Resuscitative facilities should be available.

Injectable Valium (diazepam) is not recommended as the sole treatment for psychosis or severely depressed patients. Injectable Valium (diazepam) should not be administered to patients in shock, coma, or in acute alcohol intoxication with depression of vital signs.

Physical and Psychological Dependence: Withdrawal symptoms (similar in character to those noted with barbiturates and alcohol) have occurred following abrupt discontinuance of diazepam (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). These were usually limited to those patients who had received excessive doses over an extended period of time. Particularly addictive potential individuals (such as drug addicts or alcoholics) should be under careful surveillance when receiving diazepam or other psychotropic agents because of the predisposition of such patients to habituation and dependence.

Use in Pregnancy: Use of any drug in pregnancy, lactation or in women of childbearing age requires that the potential benefit of the drug be weighed against its possible hazard to mother and child. (See Reproduction Studies.)

Management of Overdosage: Manifestations of Valium (diazepam) overdosage include somnolence, confusion, coma and diminished reflexes. Respiration, pulse and blood pressure should be monitored, as in all cases of drug overdosage, although, in general, these effects have been minimal following overdosage. General supportive measures should be employed, along with immediate gastric lavage. If a coma exists fluids should be administered and an adequate airway maintained. Hypotension may be combated by the use of Levophed (levatergine) or Aramine (metaraminol). If ataxia (vertigo) is present, ataxia and vomiting may be relieved by giving 10 mg of Valium (diazepam) orally. If ataxia is of limited value. As with the management of intentional overdosage with any drug, it should be borne in mind that multiple agents may have been ingested.

Precautions:

ORAL AND INJECTABLE: If Valium (diazepam) is to be combined with other psychotropic agents or anticonvulsant drugs, careful consideration should be given to the pharmacology of the agents to be employed—particularly with known compounds which may potentiate the action of Valium (diazepam), such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants. The usual precautions are indicated for severely depressed patients and those in whom there is any evidence of latent depression particularly by the recognition that suicidal tendencies may be present and protective measures may be necessary. The usual precautions for treating patients with impaired renal or hepatic function should be observed.

ORAL: In elderly and debilitated patients, it is recommended that the dosage be limited to the smallest effective amount to provide the desired relief of anxiety or tension (2 mg to 5 mg twice daily initially, to be increased gradually as needed and tolerated).

Injectable: Valium (diazepam) is not recommended for barbiturates and barbiturates, because increased cough reflex and laryngospasm have been reported. Furthermore, during gastroscopy the operator must be aware of this possible reaction and necessary countermeasures should be available. Until additional information on its safety and efficacy is available, injectable diazepam is not recommended for obstetrical use or in diagnostic procedures other than gastroscopy and esophagoscopy.

Injectable Valium (diazepam) has produced hypotension or muscular weakness in some patients, particularly when used with narcotics, barbiturates or alcohol. Since Valium (diazepam) may have an additive effect with narcotics, appropriate reduction in narcotic dosage is possible. Lower doses (usually 2 mg to 5 mg) should be used for elderly and debilitated patients.

The safety and efficacy of injectable Valium (diazepam) in children under age 12 have not been established.

Adverse Reactions:

ORAL AND INJECTABLE: Because of isolated reports of hemiparesis and jaundice, periodic blood counts and liver function tests are advisable during long-term therapy. Minor changes in EEG patterns, usually low-voltage fast activity, have been observed in patients during and after Valium (diazepam) therapy and are of no known significance.

ORAL: Side effects most commonly reported were drowsiness, fatigue and ataxia. Infrequently encountered were anisocoria, confusion, depression, diplopia, dysarthria, headache, hypotension, incontinence, jaundice, changes in libido, nausea, changes in salivation, skin rash, slurred speech, tremor, urinary retention, vertigo and blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances and stimulation have been reported; should these occur, use of the drug should be discontinued.

Injectable: Side effects most commonly reported were drowsiness, fatigue and ataxia. Infrequently encountered were confusion, constipation, depression, diplopia, dysarthria, headache, hiccup, hypotension, hypotension, incontinence, jaundice, changes in libido, nausea, phlebitis at injection site, changes in salivation, skin rash, slurred speech, syncope, tremor, urinary retention, vertigo and blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances and stimulation have been reported; should these occur, use of the drug should be discontinued.

Dosage and Administration:

ORAL:

Dosage should be individualized for maximum beneficial effect. While the usual daily dosages given below will meet the needs of most patients, there will be some who may require higher doses. In such cases dosage should be increased cautiously to avoid adverse effects.

Adults:
Symptomatic Relief of Tension and Anxiety States and Psychomotor States
Symptomatic Relief of Acute Alcohol Withdrawal

Adjustment for Relief of Skeletal Muscle Spasm
Adjustment for Convulsive Disorders
Geriatric Patients, or in the presence of debilitating disease

Children:

Response of varied responses to CNS-acting drugs, initiate therapy with lowest dose and increase as required. Not for use in children under 6 months.

Injectable:

Dosage should be individualized for maximum beneficial effect. In acute conditions the injection may be repeated within one hour although an interval of 4 to 6 hours is usually satisfactory. Generally not more than 30 mg should be given within an 8 hour period.
Injectable Valium (diazepam) should be injected slowly into the muscle.
Intravenous use: The solution should be injected slowly, directly into the vein, taking at least one minute for each 5 mg (1 ml) given. Do not mix or dilute injectable Valium (diazepam) with other solutions or drugs. Do not add to I.V. fluids.

Moderate Psychomotor States: Manifested by tension, anxiety, acute stress reactions, or depressive symptoms, agitation, tremor, and psychomotor states at this time.

Severe Psychomotor States: Where severe anxiety, apprehension or agitation exist alone or associated with depressive symptoms.

Acute Alcohol Withdrawal: As an adjunct to symptomatic relief of acute agitation, tremor, impending or acute delirium tremens and hallucinations.

Acute Stress Reaction: Adjustively related apprehension, anxiety and acute stress reactions are present prior to gastroscopy and esophagoscopy. Pre-anesthetic muscle spasm: Associated with local pathology, cerebral palsy, atetosis, still man syndrome or tetanus.

Status Epilepticus and Severe Recurrent Convulsive Seizures: In the comatose patient, it is recommended that the drug be given intravenously if there is difficulty in administering it slowly intravenously over the required period of time.

Preoperative Medication: To relieve anxiety and tension (If atropine, scopolamine or other premedications are desired, they must be administered in separate syringes.)
Endotracheal Intubation: To relieve anxiety and tension.

*Lower doses usually 2 mg to 5 mg, and also increase in dosage should be used for elderly or debilitated patients and when other sedative drugs are administered. (See Precautions and Adverse Reactions.)

Since the same symptomatology has been properly controlled with injectable Valium (diazepam), the patient may be placed on oral therapy with Valium (diazepam) if further treatment is required.

How Supplied:

ORAL: Valium (diazepam) scored tablets—2 mg, white; 5 mg, yellow; and 10 mg, tan—batches of 100 and 500. All strengths are available in Tel-E-Ject disposable syringes of 100 and 500. **Injectable:** Ampuls, 2 ml, boxes of 10, 50, 100, 200, 500, 1000. Each ampul contains 5 mg diazepam compounded with 10% propylene glycol, 10% ethyl alcohol, 5% sodium benzoate and benzoic acid as buffers, and 1.5% butyl alcohol as preservative.

ROCHE

Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

Dutch Physician Demonstrates Fetography

FETOGRAPHY is a relatively new method of roentgenologic examination of the fetus. In a three-year study Dr. P. F. Wiesenhaan of Haarlem, the Netherlands, performed 76 fetographies. Examples of his work are shown here and on page 1.

In Dr. Wiesenhaan's procedure two injected radiopaque contrast media are used—ethiodized oil, for outlining the skin, and hydrosoluble meglumine diatrizoate, to visualize the fetal intestines and bladder. Injection is made into the amniotic sac after an equal amount of amniotic fluid has been withdrawn, care being taken to avoid puncturing the placenta and rupturing the chorionic vessels.

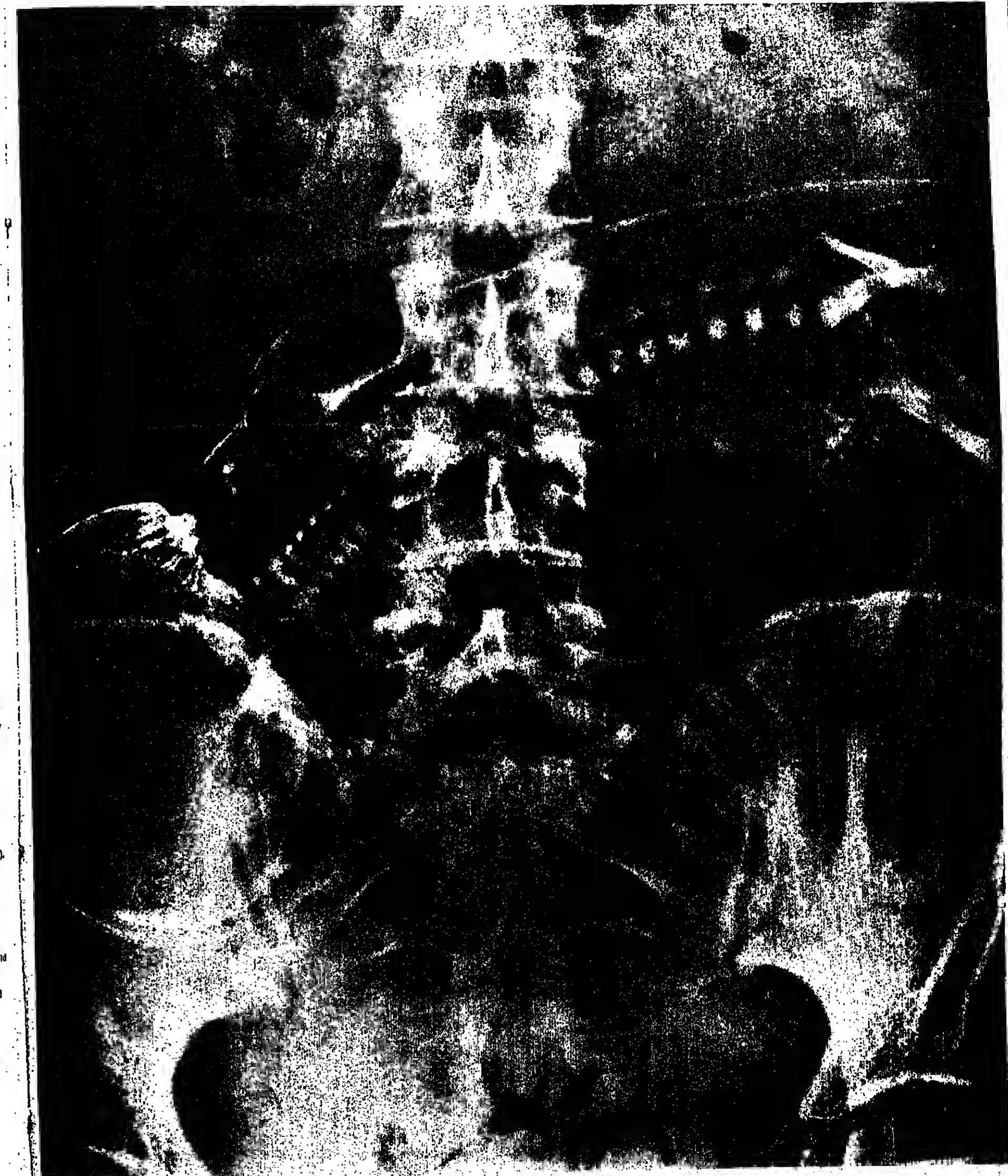
Among the indications for fetography are Rh incompatibility,

so that the condition of the fetus may be judged prior to intra-uterine transfusion; hydramnios, for the detection of congenital malformations; twins, to differentiate between mono- and diamniotic twins; and, in a rare number of cases, fetal sex determinations.

Left, a fetogram of a normal female fetus of 37 weeks' gestation. Indication was the fear of congenital malformation, as a previous child was a monster. Below, the indication was severe hydramnios in the 29th week of pregnancy in a mother with a history of diabetes. Little intestinal filling is shown, and the fetus is too large for its age. The child died soon after birth; autopsy revealed findings consistent with diabetes mellitus.



DR. WIESENHAAN



One Man...and Medicine

ARTHUR M. SACKLER, M.D.,
International Publisher, Medical Tribune



The Princess and the Porcupine Quills

Robert Rauschenberg's formal dinner for Her Royal Highness Princess Christina of Sweden was perhaps the most unusual interpretation of a black-tie party since somebody dressed a monkey in a dinner jacket and seated it next to the hostess.

—New York Times, October 29, 1972

I WAS THERE. When the taxi pulled up—or, rather, I should say, backed up—to 381 Lafayette Street, I couldn't quite fit the old brownstone house among SoHo's lofts and manufacturing buildings in with the black-tie invitation in honor of Her Royal Highness Princess Christina of Sweden. My first reaction was that I was still suffering time lag from the lost of several trips overseas. The three policemen at the door suggested that perhaps this was the right place after all, that there was a dinner party on for a princess.

It was sheer luck that I was there—and good luck at that. I had found the invitation hurled in the correspondence which piles up between trips. I had learned several weeks before, when I was in Stockholm visiting at her grandfather's palace, that she would be in New York to support the endeavor to place the New York Collection for Stockholm in the Moderna Museet.

The Artist and the Black Tie

As we entered, we circled rather warily around a girl with red eye make-up, a beaded headdress with a peacock feather, and a pink-and-green satin dress. One look around and my concept of a "black tie" dinner was knocked into a cocked hat. After being checked in as bona fide guests, we were given a piece of paper on which a helpful young lady penciled "2—table 13." A climb of the steep stairs enabled us to dispose of our coats. An infant crawled across the floor. It was Hummingbird, daughter of Penelope. Penelope who? I don't know.

The high-ceilinged rooms, the clean white walls, the beautifully varnished parquet floors were a remarkable offset to the imaginative dress of the heterogeneous gathering. Robert Rauschenberg, artist and host, did wear "black tie," but his shoulder-length collared tuxedo rested on a beautiful American Indian natural suede jacket. The invitation said "black tie" but made no reference to "decorations." His were fringes, porcupine quills, and beadwork.

Traveling With Mrs. Smith

My companion of the evening was Liz. Just a few years before she had won a beauty queen contest, yet now looked closer to 18 than 24. Every time I introduced my daughter as Mrs. Smith, I got the same reaction, starting with Rauschenberg. "A likely story if ever I heard one, but you carry it off beautifully." I gave up explanations and just enjoyed their fantasy.

This was one evening which didn't wear on; it was weird, but weirdest of all was the switch in values I experienced. The artists, in their imaginative dress, seemed to be more appropriate to the occasion; their comments were of greater substance than those of the establishment—we with our black ties, dinner jackets, and patent leather shoes. Princess Christina seemed to bridge the two, having exchanged her diamond tiara for a décolleté dress which was as bold as it was befitting. She was gracious and at ease as, with Rauschenberg's arm around her, she greeted this mixed assortment of characters.

The dinner, served with paper plates and plastic cups, was delicious: graylock (fresh salmon) from Sweden, an excellent Muscadet, and Rauschenberg's own recipe for chicken in a chili sauce with buttered carrots. Following some formal words of

appreciation by a member of the Swedish diplomatic corps (the Ambassador and the Consul General and Chargé d'Affaires were all there), Women's Lib made its appearance in the person of Jill Johnston, described by the New York Times as the "self-styled 'lesbian nationalist' who rarely goes anywhere these days without a purple and white 'Dyke' button pinned to her United States Marine Corps jacket." Her protest, interlarded virtually every other sentence with "hull—," derived from her complaint that the evening was devoted to mobilizing "patrons." She insisted that they should also have "matrons." Also, the "discriminatory fact" that only two women were represented among some 30-odd artists in the collection. In this remarkable setting she seemed even further out than the "black-tie establishment." Frank Stella was at our table, dark-complexioned, hair tied back in a bun, front teeth missing, a reflective thirtyish-year-old pixie.

New Cultures, New Contrasts

The occasion, I learned, was organized, among others, by Billy Kliver, an engineer formerly with Bell Telephone who is sponsoring a great deal of his time in advancing Experiments in Art and Technology. You could call it a weird party, but you couldn't call it a wild one. You could call it a concoct, but not a clash, of cultures. For me, the evening led to a conviction that those artists I did meet were "for real," that I had personally closed my mind some years ago to the art that followed Nicolas de Stahel, that Nevelson, Larry Rivers, Rothko, as well as Stella and Rauschenberg, had something to say. But more on that some other time. I don't know about Andy Warhol; he was there, but we didn't meet.

I guess, as physicians, we are by nature conservative. It is still difficult for me to fully comprehend a world in which one dines near Madrid with the daughter of Francisco Franco, returns to New York, then within a week to the Middle East and a dinner with a prime minister, and within days attends a party for Her Royal Highness Princess Christina of Sweden in an artist's house in New York's SoHo. As time and space are compressed, as the change in tempo and values are tearing at our common concepts, they are being articulated by what has so long been, for me, the hard-to-understand efforts of those who are, in our day, called modern artists.

EPIGRAMS—Clinical and Otherwise

We are usually mistaken in esteeming men too much; rarely in esteeming them too little.

Stanislas Leszczynski
Thoughts... on the Business of Life

FDA Head Pledges Science Will Predominate on Drugs

Continued from page 1

the FDA that the "voice of science will be heard."

"The mandate of the FDA is the regulation of drugs—not doctors," he added.

In making his pledge, the Commissioner noted that the regulatory agency "must be sensitive to the demands of the public both directly and through Congress." And, he stressed, the FDA has an equal obligation to be "sensitive to the responsibilities of the practicing physicians and... to the impact that our decisions will have not only on the rights of physicians but on the future of science and medicine."

Dr. Edwards' call for fuller collaboration between FDA and the profession included a challenge to physicians, and to pediatricians in particular, to help end the current drug anomaly in which more than half of all drugs recently approved for systemic use may not be prescribed for children—but are nevertheless so used.

"Physician Has No Choice"

Nothing that in "too many cases the physician has no choice," Dr. Edwards called on the profession to help eliminate "this dangerous double standard of drug therapy." He acknowledged that it would take courage to talk about conducting drug studies in children. "The alternative is to continue as we have too often in the past to abandon our children to the therapeutic orphanage," Dr. Edwards declared.

He emphasized that, contrary to widely held opinion, there are no Federal laws or FDA regulations that prohibit new drug studies in pediatric groups.

"But let me be perfectly clear," he continued, "I am not advocating experimental treatment of any particular group of people, young or old, sick or well. I am not

speaking in the question of ethics or the legal implications of conducting an experimental drug to a patient who is not capable of giving his own consent. These are questions that only you—organized medical groups and lawyers—can answer."

"What I am saying is this: It is not a question of whether drugs should be studied in children, but rather when, how, in whom, and under what circumstances."

Out of necessity, most of you every day are treating children with drugs not approved for therapeutic use. In effect, you are conducting drug studies. We need to do more to formalize what is already done informally. The reward will be wider application of better information for the greater benefit of children generally."



Dr. Edwards

The FDA, he declared, is committed to "the goal of advancing the New Drug Application process toward the ideal where our new drug with a potential for use in children is tested for that purpose and approved for that purpose at the same time the drug is approved for adults."

In the meantime, he urged physicians to support the FDA's new pilot project for reporting drug reactions via the experience report forms in the FDA Drug Bulletin. "A vital part of such a system requires that you tell us what's happening with the use of these drugs in your pediatric practice," Dr. Edwards stated. "As such information is provided, it is then FDA's responsibility to collect, to analyze, and to furnish you with appropriate feedback."

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...brief summaries of editorials in guest editorials in current medical journals.

Communicating Medicine

"In spite of these changing times and in spite of the demands of modern medicine, the study of medicine should be conducive to scholarship and writing. To record and to transmit information accurately and succinctly is a skill that should be basic to every branch of medicine." Yet the effect of the knowledge explosion "has been the almost total disappearance of scholarship among medical men.... Human diseases today leave no time for the humanities, and the only culture we know may be the bacteriologist's broth." In regard to medical writing, the physician "must learn from his college days, through his time in medical school, and during his postdoctoral training to write well, clearly, and concisely...."

"If as authors we are to improve medical literature, and not destroy it, we must set our faces against loose or obscure or unnecessary jargon. We must pay attention to the meaning of the words we use, ensuring that we use only words whose meanings we understand, and, so far as possible, words whose meanings others understand.... In this way we as authors may perhaps rediscover the lost tool of language. This may be difficult.... It is nevertheless the price to be paid if we wish to be worthy members of a learned profession." A. Whitley Branwood, M.D., special article, (N.Y. State J. Med. 72:2482, October 15, 1972.)

To Nibble or to Gorge?

"The pattern of ingestion of food has a considerable effect on the metabolism and body composition of experimental animals.... The findings in man are less clear-cut, but there are some indications that we may fare better on nibbling than on a gorging or conventional meal pattern.... Some studies have shown an increase of

'Genetic Prediabetics' Found To Have Capillary Variation

Medical Tribune Report

WASHINGTON—A study of subjects with diabetic parents or grandparents has disclosed that the basement membrane width (BMW) of muscle capillaries is significantly thicker in some of these persons than in normal controls of the same age, the American Diabetes Association was told here.

Further, the findings in 32 "genetic prediabetics"—all with normal glucose tolerance—showed that BMW is greater in those subjects with two diabetic parents than in those with one, it was reported by Dr. Rafael A. Camerini-Davalos, Professor of Medicine at New York Medical College. The study was undertaken to investigate

the possible role of genetic factors in the microangiopathy of diabetes.

The investigator, who stressed that all findings were preliminary, also reported that another phase of the study—seeking to throw light on the "additive significance" of glucose dysmetabolism in chemical diabetics—has shown that microangiopathy progressed as tolerance to glucose deteriorated.

The electron microscope studies were made of thigh muscle biopsies taken from 24 normal subjects, 32 prediabetics with normal glucose tolerance and a family history of diabetes, and 18 chemical diabetics with abnormal glucose tolerance, normal fasting blood sugar, and no symptoms.

Capillaries were photographed at approximately 6,000 to 8,000 magnification and 100 measurements of BMW per muscle biopsy were done, Dr. Camerini-Davalos reported.

"When the prediabetics were matched with normal control subjects according to age, sex (19 per cent) of the prediabetics were found to have a basement membrane width [significantly] above the mean for the control group of the same age," the investigator reported. "BMW was significantly different in 24 genetic prediabetics with both parents diabetic, when compared with eight genetic prediabetics with one parent diabetic and a grandparent on the nondiabetic parents' side."

Difference Not Related to Age

He added that the difference was not related to age, since the mean age for those with two diabetic parents was 27.2 years and that of the others was 28.6 years.

The mean BMW of the 19 chemical diabetics was also significantly greater (1,491 Å) than that of the 25 controls (1,250 Å), Dr. Camerini-Davalos reported. He stressed that the age of the chemical diabetics (a mean of 53 years) could have been a decisive factor in the difference of BMW from those of the controls, whose mean age was 35. But he noted that when seven controls with a mean age of 47 were compared with 10 chemical diabetics whose mean age was 49, "the difference was still significant."

Dr. Camerini-Davalos and his colleagues studied seven of the chemical diabetics whose BMW was above the mean plus two standard deviations of normal controls. In five of these, glucose intolerance was discovered to be of more than four years' duration.

Based on these observations, he continued, the team undertook a pilot study in which chemical diabetics were treated with oral hypoglycemic agents. The purpose was to see if therapy could delay or reverse BMW thickening.

The results, Dr. Camerini-Davalos reported, were "surprising." Eighteen chemical diabetic patients, with a mean age of 49 and mean duration of carbohydrate intolerance of 4.5 years, were treated either with tolbutamide 500 mg. daily or chlorpropamide 125 mg. daily for several years.

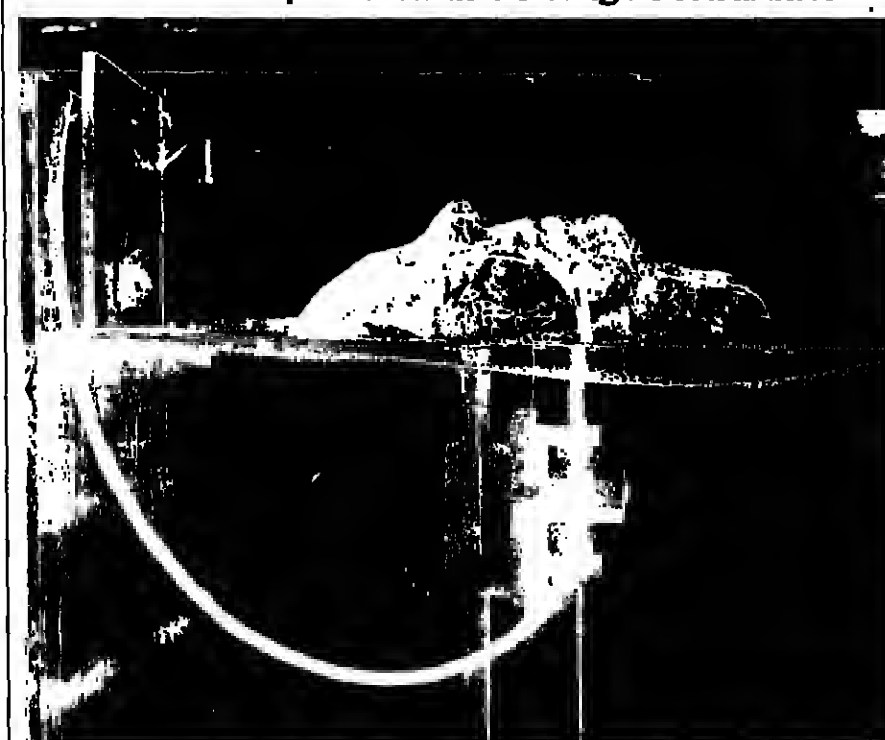
"The previously described difference between chemical diabetic patients and nor-

mal control subjects was found to be abolished by the treatment," he declared. "Our findings of the effect of the oral 'antidiabetic' compound on the delay, prevention, or amelioration of the thickening of the capillary basement membrane of chemical diabetics was surprising."

"Is this apparent over-all beneficial effect," he continued, "due to the fact that the treatment was started at an early phase, before overt diabetes? In the studies of Spiro, the beneficial effect of treatment on the glycosyl transferase activity of the renal cortex of alloxan diabetic animals, which probably reflects basement membrane synthesis, was achieved when the treatment was instituted early. Far more sequential studies in larger groups of subjects will be necessary before these findings suggesting a prevention, delay of progression, or amelioration of the diabetic microangiopathy by early treatment can be accepted."

Coauthors were Drs. James B. Bloodworth, Jr., Balduz Limburg, Arthur L. Gordon, Harold S. Cole, Carlos Velasco, and Weiner Oppermann.

Phantom Helps Determine Dosage Distribution



Dosage distribution of radiation can be more accurately determined with the use of a new water phantom developed at the University of Kentucky's Albert B. Chandler Medical Center. The phantom is a water-filled clear plastic mold of the body area to be treated. The tube entering the phantom is a small radiation-measuring chamber.

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Naturally, an imitation does not equal the original. Synthetic chemicals often lack some vital qualities that may thus be lacking in the natural medicinal.

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discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards. As with all anticholinergic drugs, an inhibiting effect on lactation may occur.

Precautions: In elderly and debilitated, limit dosage to smallest effective amount to preclude development of ataxia, oversedation or confusion (not more than two capsules per day initially; increase gradually as needed and tolerated). Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: No side effects or manifestations not seen with either compound alone have been reported with Librax. When chloridazepoxide hydrochloride is used alone, drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—oil infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally with chloridazepoxide hydrochloride, making periodic blood counts and liver function tests advisable during protracted therapy. Adverse effects reported with Librax are typical of anticholinergic agents, i.e., dryness of mouth, blurring of vision, urinary hesitancy and constipation. Constipation has occurred most often when Librax therapy is combined with other spasmolytics and/or low residue diets.

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Doctors' Debate

MEDICAL TRIBUNE frequently receives extensive and well-documented communications from physicians on current subjects of controversy or those of great current medical interest. We invite contributions in these areas for presentation in this new feature.

The Tuskegee Syphilis Study

Editor, MEDICAL TRIBUNE:

MEDICAL TRIBUNE deserves the highest commendation for its coverage of the Tuskegee Syphilis Study. I am most grateful to you for your series, from which I first heard about this gruesome medical atrocity, and for having been kept informed of current developments and reactions of medical men throughout the world.

Doctor Sackler's editorial of September 9 was by far the most penetrating and most vigorous evaluation of the Tuskegee Syphilis Study I have seen anywhere. His characterization of the TSS as a "horror of human experimentation" and "a nightmare turned into reality," his condemnation of the project, his moral indignation, were appropriate.

The first two parts of your series aroused my intense curiosity, and I have since obtained all of the available original publications on the TSS. I was fortunate in being able to get a 1933 edition of J. E. Moore's *Modern Treatment of Syphilis*. The later edition of 1941 was already in my possession, left over from my later years. A few weeks before, when I was in Stockholm visiting at her grandfather's palace, that she would be in New York to support the endeavor to place the New York Collection for Stockholm in the Moderna Museet.

The Artist and the Black Tie

As we entered, we circled rather warily around a girl with red eye make-up, a beaded headdress with a peacock feather, and a pink-and-green sari dress. One look around and my concept of a "black tie" dinner was knocked into a cocked hat. After being checked in as a guest, we were given a piece of paper on which a helpful young lady pencilled "2-table 13." A climb of the steep stairs enabled us to dispose of our coats. An infant crawled across the floor. It was Hummingbird, daughter of Penelope. Penelope who? I don't know.

The high-ceilinged rooms, the clean white walls, the beautifully varnished parquet floors were a remarkable effect to the imaginative dress of the heterogeneous gathering. Robert Rauschenberg, artist and host, did wear "black tie," but his shoulder-length coiffure rested on a beautiful American Indian natural suede jacket. The invitation said "black tie" but made no reference to "decorations." His were fringes, porcupine quills, and beadwork.

Travelling With Mrs. Smith

My companion of the evening was Liz. Just a few years before she had won a beauty queen contest, yet now looked closer to 18 than 24. Every time I introduced my daughter as Mrs. Smith, I got the same reaction, starting with Rauschenberg, "A likely story if ever I heard one, but you carry it off beautifully." I gave up explanations and just enjoyed their fantasy.

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The dinner, served with paper plates and plastic cups, was delicious gravlox (fresh salmon) from Sweden, an excellent Muscadet, and Rauschenberg's own recipe for chicken in a dill sauce with buttered carrots. Following some formal words of

like to point out, however, aside from the utter immensity of the racist human experimentation, that the TSS was a tragic and wasteful failure. After 40 years of coercion, harassment, cajoling, and threatening of 430 poor and uneducated black men, the experimenters cannot claim that the survivors were really untreated syphilitics.

Sitting at their handsome desks in cramped offices in Washington, D.C., the United States Public Health Service bureaucrats failed to reckon with human re-

"I can state unequivocally that arsenicals were easy to administer, that there were no catastrophic side effects, and that they were an effective antineoplastic therapy...."

sourcefulness. Denied treatment by the USPHS, the victims got it elsewhere. The last published report in 1964 (*Archives of Internal Medicine*) estimated 96 per cent of the surviving syphilitics had received arsenicals—i.e., antineoplastic therapy, and many "self-styled" tests had gotten enough to be goes anywhere alive.

and while "Dy" (unpublished) in 1971 United States. But one had had anti-syphilitic, later, in the final analysis, the sentence with "but" as they do, that 74 complaint that the "because of having demobilizing" "prior, and immunity to the they should also have 74 black men had "discriminatory fact" and "intuitive to were represented as a therapy outside of lists in the collected" of the USPHS setting she seemed to the "black-tie" and ARONOWITZ, M.D. was at our table, dark Angeles, Calif. tied back Indian fashion, a reflective thirteenth.

New Cultures

The Tuskegee project is interesting because in the occasion, I have seen and I among others, by Billy of inductees at formerly with Bill's friend to have pos- spending a great deal which we got some winning Experiments in human prior treat- ogy. You could call it in the South in you couldn't call it a standard of syphilis tures. For me, the even pain, expanse, and tion that those artists' rds involved in the real," that I had persons with injections, it some years ago to three could well have Nicolas de Stahl, theoretically reason- Rivers, Rothko, as via Tuskegee study. Rauschenberg, had so clearly disappeared more on that some other of penicillin was about Andy Warhol; generally available. didn't meet. e study should have

I guess, as physician conservative. It is still fully comprehend a w dines near Madrid with Francisco Franco, retu then within a week to a dinner with a prime n days attends a party for Princess Christina artist's house in New time and space are change in tempo and vi our common concepts, ticated by what has so tha hard-to-understand who are, in our day, ca

EPIGRAMS—Clinical
We are usually mist-
aken too much; rat-
her too little.
Sta-
Thoughts
© 1973 National Tribune

Cancer Detection



The Missouri Regional Medical Program has developed a self-palpating cancer detector, shown above. After use, the pipet is inserted into a lab for analysis and the woman and her physician are notified of the results in order to ensure proper follow-up if an abnormal cytology has been found.

ence, it seems to me most unfortunate that the National Medical Association has characterized the whole experiment as "racism." Considering the art of syphilis treatment in 1932, prior to penicillin, it was then reasonable. I'm sure many similar treatment versus no-treatment experiments were, and still are, being carried out in many groups who are not black.

As for failure to discontinue the experiment postpenicillin, by the time penicillin became freely available in the late 1940s, the Tuskegee Experiment was already 15 or more years old. That's plenty of time for an organization of clerks, nurses, statisticians (and no doubt a few rapidly rotating USPHS medical officers) in have created for their little bureau a life of its own.

"I believe the Tuskegee experiment's real lesson is that it gives us a glimpse of bureaucratic medicine in operation and in dimensions we can easily comprehend."

I believe the Tuskegee experiment's real lesson is that it gives us a glimpse of bureaucratic medicine in operation and in dimensions we can easily comprehend. I must admit that I do not advocate the abolition of all bureaus. Obviously a mass society must have governmental bureaus to conduct its affairs. But all governments should routinely raise the question whether need still exists for bureaus long established.

JOSEPH W. STILL, M.D., M.P.H.
Arcadia, Calif.

Editor, MEDICAL TRIBUNE:

Note is taken of the emphatic condemnation on part of the several Japanese physicians—i.e., Doctor Soda, Doctor Takami, et al.—in regard to the Tuskegee syphilis study.

In 1939 the Japanese Army encountered serious difficulties with so-called epidemic hemorrhagic fever in Manchukuo. During the Korean War the same was true with the American Eighth Army, and as a medical officer involved at the height of several epidemics, a rather direct and uninhibited earlier experimental effort made by Japanese investigators and involving Chinese "volunteers" came to our attention.

Unfortunately, most of this considerable amount of Japanese work involving attempted transmission as well as aerial inspection in the most fundamental sense was understandably not available to us.

Most of us in Korea charged this off to Oriental pragmatism, but in the light of the rather sanctimonious murmurs from Tokyo this seems at least a little bit relevant.

RICHARD B. HUNTER, M.D.
Dallas, Tex.

NBT Test Evaluated

ATLANTIC CITY, N.J.—The nitroblue tetrazolium (NBT) test, which seems to be useful in differentiating serious bacterial infections from other fever-causing diseases, was "a poor predictor of streptococcal versus nonstreptococcal pharyngitis" in outpatient pediatric clinics, the Interscience Conference on Antimicrobial Agents and Chemotherapy was told.

Drs. J. V. Randall, V. Perrillo, and J. O. Hendley, of the University of Virginia School of Medicine, evaluated the test with 81 patients, choosing pharyngitis as a testing area because of the availability of comparative throat swab cultures for determining whether the illness was bacterial.

They reported that 37 of the patients had group A beta hemolytic streptococci in their throats, but only 14 of them had positive NBT tests. Forty-four had negative throat cultures, but six of these also had positive tests.

Percutaneous Catheters

HOUSTON, TEX.—"Distinct" advantages of percutaneous sheath cardiac catheterization in infants and children, compared with the surgical exposure of vessels for catheter insertion as well as percutaneous cardiac catheterization not utilizing a sheath, were emphasized by investigators at the Baylor College of Medicine and Texas Children's Hospital.

Describing 565 consecutive femoral vessel catheterizations using an indwelling sheath, they said that advantages included "the ability to use the same vessel for repeat studies, small incidence of arterial complications, ease of making many changes in catheter as well as ability to use any type of catheter." In addition "there is a greater chance of entering the left side of the heart with a percutaneous femoral venous catheter, which, in many patients, may avoid performance of a retrograde arterial procedure."

The investigators, whose report appeared in the *American Journal of Cardiology*, were Drs. William H. Neely, Charles E. Mullins, Robert L. Williams, Thomas A. Vargo, and Dan G. McNamara.

Baby Boom in Australia

CANBERRA—Australia is currently experiencing a baby boom. Figures released by the Australian Statistics Bureau show that the birth rate increased by 5.24 per cent last year, compared with a 5.97 per cent rise for the preceding three years.

AV Block in Neonate

TOKYO — In selected cases of congenital atrioventricular conduction block with congestive failure in the newborn, pacemaking with a catheter electrode through the umbilical vein is a simple and effective method of treatment, it was reported.

Successful results can be achieved with bradycardia by pacemaking immediately after delivery, it was said, and also in patients where only relatively slight cardiac anomalies are present.

Since many newborns with heart-block suffer not only from bradycardia but also from cardiac anomalies, the success of this method of treatment depends primarily on the severity of cardiac anomalies, the fifth annual meeting of the Pacific Association of Pediatric Surgeons was held by Drs. Toshio Mitsui and Yoshiaki Tsuchida, of Tokyo University School of Medicine.

Thymus Transplant in Child

MELBOURNE, AUSTRALIA—A two-year-old child with di George's congenital aplasia of the thymus syndrome is Australia's first recipient of a thymus transplant. Extensive tests showed a total defect of cellular immunity, and no evidence of T-cells in the blood.

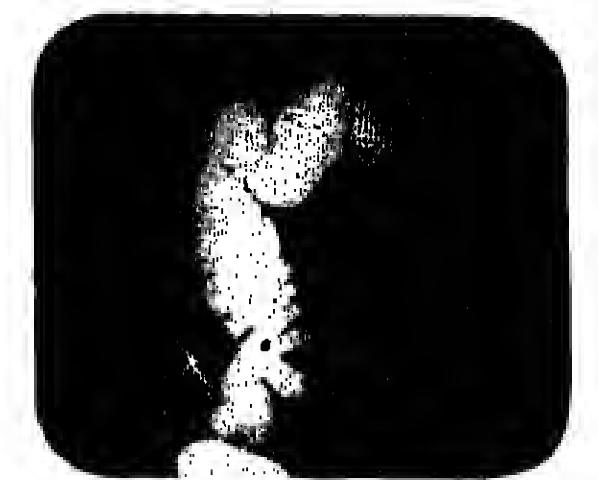
He received thymus tissue from a fetus aged 14 to 16 weeks, available after therapeutic abortion.

G.I. FORUM

A CURRENT REVIEW OF INVESTIGATIONS IN GASTROENTEROLOGY

The Great Impersonator

The patient with irritable bowel syndrome—the most common G.I. complaint seen by the gastro-



terologist—is observed by virtually every medical practitioner except the pathologist. Though no primary pathologic change has yet been demonstrated, irritable bowel syndrome can be confused with other diseases. It has been referred to as the "great impersonator" because its multiple symptoms can mimic many other disorders—pancreatitis, myocardial infarct, endometriosis and even a surgical abdomen. No matter what complaints the patient has as a result of irritable bowel syndrome, excessive anxiety can be a contributing factor.

Anxiety, ancestors, milk

The role of excessive anxiety and other emotions in producing G.I. distress has been amply documented, but another factor has recently come to light—that of lactose intolerance due to low-lactase activity.² Milk intolerance is now thought by some investigators to be a contributing factor in the development of certain G.I. symptoms—including some associated with irritable bowel syndrome. Widespread interest in this phenomenon has led to many investigations. The general consensus is that low lactase levels appear to be normal in most adults all over the world; Scandinavians and descendants of northern Europeans being the major exceptions.

One study was conducted among neighboring tribes in Uganda.³ When given lactose, many of those who were vegetable eaters and seldom drank milk developed G.I. symptoms including diarrhea. On the other hand, when people of the dairy-herding tribes were given lactose, they seldom showed these symptoms. Findings from Nigeria were similar.⁴ Lactase deficiency appeared commonly in non-dairy farming groups and less commonly in pastoral tribesmen.

Infants and children up to approximately age three throughout the world seem to have no trouble digesting milk—presumably because of normal lactase activity. Studies in many countries have indicated that malabsorption of lactose is very frequent after early childhood.

The tolerant intestine—A 5000-year-old mutation

But what about the many thousands of people who can drink milk with impunity? It has been suggested that the answer might lie in the history of dairy



farming, thought to have begun about 5000 years ago.⁵ In areas around the Nile Basin, the Sahara and in certain parts of northern Europe, people began to raise cattle and to drink milk beyond the normal weaning age. In general, the descendants of these early herdsmen are today's milk drinkers. It has been postulated that the persistence of high levels of lactase beyond early childhood is a genetic mutation—a response to generations of milk-drinking ancestors.

People who are intolerant of milk would seem to be more normal in terms of humanity at large. In their own countries, eating according to traditional dietary patterns, probably no problems would arise; but many live in the United States. Here, milk drinking is part of the culture and is urged for people of all ages. Often, gastrointestinal symptoms result from following this cultural edict. Perhaps it would be more suitable to recommend fermented forms of milk such as yogurt and cheese. These foods are often a normal part of the non-milk drinker's diet and apparently do not provoke distressing symptoms.

References: 1. Hellerman, E. W. *Amer. J. Gastroenterol.*, 43:468, 1965. 2. Bayless, T. M.; Paige, D. M., and Ferry, G. D. *Gastroenterology*, 60:605, 1971. 3. Cook, G. C., and Kujubel, S. K. *Lancet*, 1:725, 1966. 4. Kretschmer, N., et al. *Lancet*, 2:392, 1971. 5. Kretschmer, N. *Gastroenterology*, 61:805, 1971.

The Logic of Librax

Milk may not be a factor in your patient's irritable bowel syndrome, but more often than not, excessive anxiety plays a role. In certain gastrointestinal disorders an appropriate approach to therapy, including Librax, can be of particular value.⁶ Anticholinergics alone are unlikely to aid recovery if the patient's undue anxiety is not reduced. Librax combines in a single capsule the well-known antianxiety action of Librium® (chlordiazepoxide HCl) with the antisecretory/antispasmodic action of Quazan® (cldinium Br) to help restore the colon to more normal function.

Appropriate dual-action therapy

The action of Librium helps relieve excessive anxiety resulting from emotional stress and may thus help reduce any resulting overreaction of the susceptible colon. At the same time, the action of Quazan, a dependable anticholinergic, helps to lessen excessive motility of the colon and relieve spasm and associated pain.

Up to 8 capsules daily in divided doses

For optimum response, dosage should be adjusted according to each patient's requirements—1 or 2 capsules, 3 or 4 times daily. Librax, along with your counseling, can help in the medical management of your patients with irritable bowel syndrome.

*Labbardi, R. "Psychopharmacotherapy in Gastrointestinal Disease," in Pletscher, A., and Marino, A. (eds.): *Psychotropic Drugs in Internal Medicine*, Amsterdam, Excerpta Medica Foundation, 1970, pp. 109-114.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Symptomatic relief of hypersecretion, hypermotility and anxiety and tension states associated with organic or functional gastrointestinal disorders; and as adjunctive therapy in the management of peptic ulcer, gastritis, duodenitis, irritable bowel syndrome, spastic colitis, and mild ulcerative colitis.

Contraindications: Patients with glaucoma; prostatic hypertrophy and benign bladder neck obstruction; known hypersensitivity to chlordiazepoxide hydrochloride and/or cldinium bromide.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering Librium (chlordiazepoxide hydrochloride) to known addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to these seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards. As with all anticholinergic drugs, an inhibiting effect on lactation may occur.

Precautions: In elderly and debilitated, limit dosage to smallest effective amount to preclude development of ataxia, oversedation or confusion (not more than two capsules per day initially; increase gradually as needed and tolerated). Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

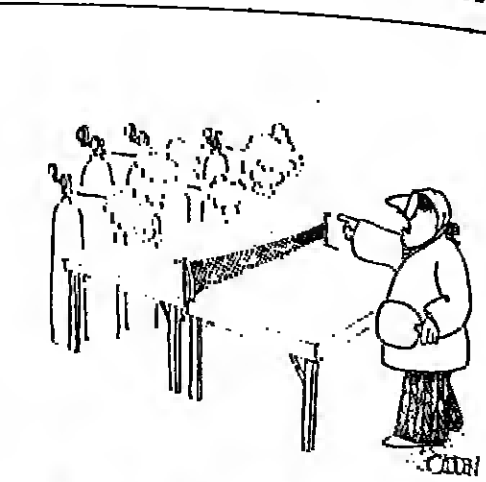
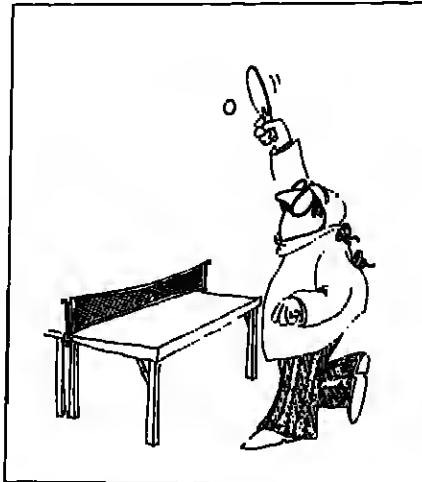
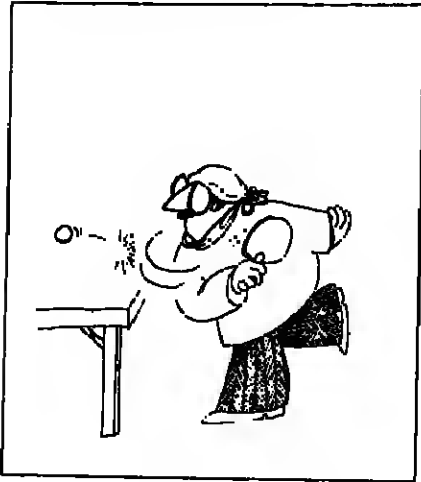
Adverse Reactions: No side effects or manifestations not seen with either compound alone have been reported with Librax. When chlordiazepoxide hydrochloride is used alone, drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extropyrindol symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally with chlordiazepoxide hydrochloride, making periodic blood counts and liver function tests advisable during protracted therapy. Adverse effects reported with Librax are typical of anticholinergic agents, i.e., dryness of mouth, blurring of vision, urinary hesitancy and constipation. Constipation has occurred most often when Librax therapy is combined with other antispasmodics and/or low residue diets.

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by Olden

Physicians Hail National Plan For Combating Hypertension

Continued from page 1
will respond "warmly" to the program.

Dr. Campbell Mases, medical director of the American Heart Association, endorsed the program as a "top-priority effort."

Their full comments follow:

Dr. Moyer: The thrust towards identification and treatment of essential hypertension, in my opinion, is an approach toward the development of an over-all and coordinated national plan that is long overdue. One of the major problems in the delivery of health services today is fragmentation of effort. Therefore, if the program for identification and treatment of hypertension is sufficiently effective to be used as a model, this will be a major advance in the treatment of many kinds of diseases—especially those for which effective treatment is available, as is the case with essential hypertension.

It has now been shown beyond a reasonable doubt that specific treatment with specific antihypertensive medication is not only effective in preventing or greatly reducing mortality due to the disease, but is also quite effective in reducing morbidity resulting from hypertension and its complications. Consequently, it is timely that a major effort should be made to identify and treat patients with hypertensive illness.

Common Effort Important

Dr. Cooper has emphasized the importance of bringing the various governmental agencies together in this common effort. Many of the agencies related to the delivery of health services have programs that are ongoing but are frequently unaware that another agency might be reducing their effort. This anticipated unifying joint effort will be quite important in bringing these agencies into communication with each other.

These same conclusions apply to the local community effort. Many different scientific and social agencies are working independently—often out of communication with each other. In addition, the physicians in the community are often working independently and autonomously. A giant step will have been made if models can be developed which communities—i.e., the consumer—can follow in coordinating their activities related to the identification and treatment of hypertension. This, then, may serve as a model in the community for the delivery of other health services in the treatment of many categories of disease.

It is my opinion that the medical profession will be the whole respond in a positive manner.

As I see the over-all development, a major contribution will be improvement in communication and planning among the major Federal health agencies. In addition, bringing of the medical and allied health professions into joint planning cannot be anything but helpful.

However, the main problem will be at the community level. This will be the matter of bringing the various health services together with the various professions in



Dr. Freis



Dr. Mosby

joint planning and the execution of the plans.

In a community which at the moment has many professional societies and facilities operating autonomously, where is the leadership coming from that will bring all of these facilities and efforts together in a joint venture? Whenever this is done, the independence and autonomy of the individual organizations and units must be sacrificed in part to achieve a cohesive and over-all operation. Can this be accomplished?

In some communities where a spirit of competition and advancement is dominant, this will be accomplished. In other communities where the health units and programs are more oriented to the vested interest and ego satisfaction of the individuals involved rather than to the over-all good of the community, then this effort is bound to fail. The latter must be avoided if at all possible.

I should like to conclude with a sensitive observation. A symposium, the first Hahnemann Symposium on Hypertension, was held in Philadelphia in 1959. At that time a major segment of researchers throughout the world gathered here to discuss the then known and established facts that were related to the etiology and treatment of hypertension. Major breakthroughs had just been accomplished, and for the first time effective agents for reducing blood pressure had been discovered during the previous 10 years. There was little doubt among the investigators that control of blood pressure was reducing morbidity and mortality among the patients with more serious hypertension, especially those with so-called malignant hypertension. Yet there were no solid statistics to support the conclusions that, beyond a reasonable doubt, patients' lives were being prolonged by antihypertensive therapy when their pretreatment diastolic blood pressures were less than 120 but more than 105 mm. Hg.

Treatment Prolongs Life

Over the past 10 years, however, various studies and especially the Veterans Administration study under the direction of Dr. Edward Freis have proved beyond a doubt that for patients in this category of severity as well, treatment prolongs life and reduces morbidity. Although the investigators who participated in the Hahnemann symposium were already convinced that this was the case, solid facts were lacking.

Now, the data supporting these conclusions are available, and this has made the difference—i.e., the justification of a



A screening program for hypertension directed by Dr. Frank A. Flimery, above, head of Georgetown University's Cardiovascular Group at D.C. General Hospital, was part of an earlier NIH-supported hypertension detection and treatment program.

national program such as has been reviewed by Dr. Cooper.

Dr. Laragh: Dr. Cooper's statement about high blood pressure makes it clear that the Federal Government is well aware of the significance of the problem to national health. Moreover, the Federal authorities recognize that right now we really can do something to control high blood pressure and its devastating consequences.

Intermediary Steps Needed

Personally I believe that while we are very close to cracking the high blood pressure problem, several intermediary steps are necessary before we can initiate a massive national screening and long-term treatment program involving many million people. First of all, at present there is not enough good information on how to screen effectively and what criteria to use, nor has a solid base of facilities been organized for treatment of these millions. Moreover, there is no general agreement on whether or not such a found hypertensive should have a general medical work-up and by whom.

Over and above this, more research is still necessary before screening and treatment programs can be accurately programmed. We are very close, but we are not there yet. Thus, recent studies such as those at our Federally supported Hypertension Center make it clear that essential hypertension is not homogeneous etiologically or prognostically, so that a standard treatment regimen might actually be detrimental to some patients. Thus, it is likely that treatment programs will have to be individualized.

In this regard it is generally recognized that antihypertensive drugs, while extremely valuable, are far from perfect. There are certain more effective and more palatable drugs for high blood pressure that are generally available outside of the United States. The development and release of these drugs in the U.S. have been prevented by conflicts between the commercial goals of the pharmaceutical industry and the survival instincts of an FDA which has become totally protection-oriented.

This problem will not really be solved until this crossfire is subordinated to a mechanism which truly considers the

rights of as well as the hazards to the citizenry. Also, it seems a pity that we seem to require the elaborate study of drugs that have already been given to countless humans for many years outside of the U.S.

Dr. Cooper's awareness of the total problem and of our ongoing capabilities to deal with it are gratifying and commendable. I agree that a broad program of education is an important first step. This should be linked with intensified research and expanding pilot studies so as to develop guidelines for increasingly broad screening and treatment programs as soon as possible. However, we must not forget that the problem is not yet fully solved and that better diagnostic methods and with them better treatments could be a reality for the immediate future.

Dr. Freis: The program on hypertension outlined by Dr. Cooper is a major challenge to our health care delivery system. It is an important and timely step and has a great likelihood of success with Dr. Cooper's excellent leadership.

Dr. Sokolow: I believe the program to be most important and, as a matter of fact, I am a member of the National Hypertension Advisory Committee. I believe that the medical profession will react warmly and strongly to it, because the objective is information and education of the physician and patient and a vigorous effort to improve patient care.

Dr. Moser: The American Heart Association is represented in the over-all planning of the program, which we recognize as a top-priority effort.

We particularly applaud that part of the project directed at public education, and we plan to participate in this aspect of the program. To this end, we will run regular television spots—similar to the anti-smoking spots we ran in the past—on the importance of checking with the doctor to identify high blood pressure.

Lord Snow Propounds a Doctrine of 'As If'

Continued from page 1

principle the reverence for each individual life."

The speaker was Lord C. P. Snow, eminent British physicist, humanist, and novelist, whose lecture, "The Hospital as a Humane Institution," was the main event at dedication ceremonies for a new 188-bed wing at St. Barnabas Hospital for Chronic Diseases here.

Lord Snow addressed himself to the "biomedical ethical dilemmas" that confront the medical profession today and that will, he predicted, become even more profound in the future.

Discussing the extreme loneliness of each individual in serious illness, especially when near death, he observed that this is "one of the limits of the human condition—each one of us dies alone." It is difficult, he said, to find a practical solution to this in the face of the increasing technological complexities of medical care.

"Surrounded by all the apparatus of a modern hospital, nearly all of which most patients don't begin to understand, and passively subjected to incomprehensible tests, that passive solitary human being is frightened." The "waits of fear" in a hospital climate cannot be entirely avoided, "but perhaps we can prevent them chilling us too much."

"Technology," Lord Snow commented, "often presents us with great benefits with one hand and knives us pretty sharply with the other." Medical technology has reduced mortality and conquered many diseases, but it has also presented us with a population growth that is "perhaps the greatest mass problem that has ever faced the human race." Surgery can now be performed "with a new order of skill" and many diseases can be cured, but "psychologically, when in medical care, we are likely to be more anxious and disturbed than our fathers were."

"No Substitute for One Good Doctor"

To some degree, he declared, the patient's fears and loneliness can be assuaged by being in the hands of a single good doctor of old times. "In many conditions, most of all in those when one is face to face with mortality, there is no substitute for one good doctor. One doctor who knows me." Empathy "can give more comfort than anything that medicine can do."

While this cannot be taught, Lord Snow suggested, if the potentiality of empathy exists, "then it can be encouraged by those who have possessed it and have tried to express it in words."

There ought to be, he said, "a literary component running through the course of a medical education."

"I should include the major writers, who have tried to come to terms with the varieties of human personality, with the problems of responsibility, problems which have bedeviled men since they became self-conscious, and which are going to become sharper still."

There are signs, Lord Snow said, that in small ways indicate that "we do have a reverence for the individual life." Abolition of capital punishment in Britain and in the United States "is a sign of increasing sensitivity to the value of, if you like, the sacredness of human life." Yet, since 1914, "mainly through the activity of the most advanced countries," nearly 150,000,000 human beings "have died violent deaths, many in war, some in torment, many through planned starvation."

"Despite all the evil in us, though, despite what in practice is more dangerous than evil—our capacity to be affectless—there is just a little to build on," he continued. "There is a vestigial and struggling awareness of the sanctity of life."

"I suspect it is vitally important—vital in the most literal sense—for doctors to proclaim this awareness. It is some sort of

U. Chicago Gets Grant
CHICAGO—The University of Chicago has received a grant for \$495,660 to establish a Center of Radiologic Image Research to increase diagnostic accuracy in radiology and nuclear medicine.

guide to some of the ethical dilemmas which medicine faces now, and will face to an extent difficult to imagine by the end of the century."

Lord Snow told the story of a surgeon who, at an international conference, discussed an operation that was extremely risky and arduous for the patient to endure, and who said: "We do not advocate nor are we embarking on any therapeutic regime. It is an experiment."

Statement "Reflects Indifference"

This statement, Lord Snow commented, "reflects the indifference and inhumanity within our society. 'If we attempted to act as if the reverence for individual life was a first principle, no such remark and no such surgical procedure would be permissible. It is primarily for doctors to make it harshly clear that it is not permissible.'"

"If we believe, or even attempt to believe, in the significance of each individual life," Lord Snow continued, "then we have some guidelines. Human beings are equal in death; don't we have to act as though they are equal in the sufferings of the flesh?"

He went on to discuss "future disquiet, conceivably graver ones." Among them,

he said, will be those resulting from our growing knowledge of human genetics and the possibility of genetic manipulation. The first application of genetic engineering, he predicted, "would almost certainly be to eradicate the grosser genetic misdirections—those which produce dystonia or spina bifida or mongolism or other forms of fearful suffering."

But he warned that "if you could remove bad genetic instructions you'd be likely to be able to engineer other instructions that some people would think good."

"That is not a consoling thought," he reflected. "For I can't think of any individual people who could be trusted with such power. Or any society wise enough to make such a decision...."

"Well, at the worst, that possibility is far in the future. It is just as well, however, to keep a certain wariness."

Meanwhile, he urged, we must hold fast to our basic human faith. "Each individual human life is significant. You doctors, who have seen men in their naked loneliness, know that as well as anyone on earth. In the face of the shocks that are bound to come, you will have to help and lead us all, in cherishing and restating that final core of human faith."



Born in Leeuwarden, the Netherlands, J. L. C. Schroeder van der Kolk (1897-1962) received his medical degree at Groningen University. After serving as Professor of Anatomy and Physiology at the University of Utrecht he became governor of the psychiatric institution Willem Arsz Stichting, where he introduced humane and scientifically sound methods for treating the insane. He was instrumental in the passage of the first Lunacy Act in 1841.

The Netherlands issued the stamp in 1960 to honor World Mental Health Year. 1972 is the 175th anniversary of Kolk's birth.

Text: Dr. Joseph Kler
Stamp: Minkus Publications, Inc., New York



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CONTRAINDICATIONS: Proven or suspected pheochromocytoma; hypersensitivity to Ismelin. Do not use with MAO inhibitors. **WARNINGS:** Ismelin is a potent drug and can lead to disturbing and serious clinical problems. Warn patients not to deviate from instructions and about the potential hazards of orthostatic hypotension, which can occur frequently. To prevent fainting, patients should sit or lie down with onset of dizziness or weakness, which may be particularly bothersome during initial dosage adjustment and with postural changes. Postural hypotension is most marked in the morning and is accentuated by hot weather, alcohol, or exercise. Warn patients to avoid sudden or prolonged standing or exercise while taking Ismelin. Concurrent use with repressors may cause excessive postural hypotension, bradycardia, and mental depression. If possible, withdraw therapy 2 weeks prior to surgery to avoid possible vascular collapse and to reduce hazard of cardiac arrest during anesthesia. If emergency surgery is indicated, administer preanesthetic and anesthetic agents cautiously in reduced dosage with oxygen, epinephrine, and vasopressors with extreme caution because patients on Ismelin may have a greater propensity for cardiac arrhythmias.

Febrile illness may reduce dosage requirements. In frank congestive heart failure not due to hypertension, Ismelin is not recommended. Due to catecholamine depletion and increased responsiveness to norepinephrine, special care is required when treating patients with a history of bronchial asthma, since the condition may be aggravated.

Use in Pregnancy: The safety of Ismelin for use in pregnancy has not been established; therefore, this drug should be used in pregnant patients only when, in the judgment of the physician, its use is deemed essential to the welfare of the patient. **PRECAUTIONS:** Give very cautiously to hypertensive with (a) renal disease with nitrogen retention; (b) coronary disease with insufficiency or recent myocardial infarction; (c) cerebral vascular disease, especially with encephalopathy; and (d) rising BUN levels. Give with extreme caution to those with severe congestive failure. Watch for weight gain or edema in patients with incipient cardiac decompensation. If digitalis is used with Ismelin, remember that both drugs slow the heart rate. **Appetite suppression** (e.g., amphetamines), mild stimulants (e.g., ephedrine, methylphenidate), and tricyclic antidepressants (e.g., imipramine, nortriptyline, doxepin) may decrease the hypotensive effect of Ismelin. With one week after discontinuing MAO inhibitors before starting Ismelin. **Peptic ulcers** or other chronic disorders may be aggravated by a relative increase in parasympathetic tone. Periodic blood counts and liver func-

tion tests are advised during prolonged therapy. **ADVERSE REACTIONS:** Frequent reactions due to sympathetic blockade—dizziness, weakness, lassitude, syncope. Frequent reactions caused by unopposed parasympathetic activity—bradycardia, increase in bowel movements, diarrhea (which may be severe and require discontinuation of the drug). Other common reactions— inhibition of ejaculation, fluid retention, edema, congestive heart failure. Less frequently—dyspnea, angina, nausea, vomiting, nocturia, urinary incontinence, dermatitis, scalp hair loss, dry mouth, rise in BUN, ptosis of the lids, blurring of vision, periorbital edema, myalgia, muscle tremor, mental depression, chest pains (angina), chest parasthesias, nasal congestion, weight gain, and edema in susceptible individuals. **DOSE AND ADMINISTRATION:** Initial dosage should be low and increased gradually by small increments. **Before starting therapy, consult complete product literature.** **HOW SUPPLIED:** Tablets, 10 mg (pink, scored) and 25 mg (white, scored); bottles of 100 and 1000.

CIBA Pharmaceutical Company
Division of CIBA-GEIGY Corporation
Summit, New Jersey 07901

C I B A

What Diphtheria Epidemic Taught the Professionals

Continued from page 1

pharyngitis, the number of throat swabs was enormous. He now feels he knows "the best system you can find for pathologic diagnosis of diphtheria. You can quote me on that."

Enter Dr. William T. Kniker, head of the pediatrics immunology-allergy section of the connecting and connected University of Texas Medical School at San Antonio. It is due to him that the epidemic may have developed knowledge in the treatment of glomerulonephritis.

"A silver lining" of the epidemic, he calls it.

Re-enter Dr. Richard V. McCloskey, then head of infectious diseases in medicine at the medical school. Correspondence he initiated with Rumanian physicians added to knowledge about the character of the epidemic.

The laboratory relied on methylene blue stain, Albert's stain, Loeffler's plate, tellurite plate, and blood agar for preliminary diagnosis. Dr. McCracken told MEDICAL TRIBUNE.

If the results pointed to Corynebacterium diphtheriae, biochemical studies were carried out. If the presence of the diphtheria organism was thus verified, toxigenicity—yes or no—was determined with the in vitro Elek plate method.

Methylene-blue staining of a throat smear—performed and interpreted by house staff—gave only a rough idea of the presence of diphtheria. Though it is quick to perform—it takes only 50 seconds—its usefulness is limited because the normal diphtheroids in the throat that it brings out are difficult to distinguish from the disease's culprit, C. diphtheriae. Moreover, the organism responsible for non-life-threatening Vincent's angina resembles that for life-threatening diphtheria. "This is a very real problem," says Dr. McCracken, "because we had many patients who had both."

The Albert stain of a smear—carried out and interpreted in the laboratory because it requires greater expertise—can get physicians closer to certainty in a matter of minutes.

But only the cultures bring physicians near definitiveness. However, recognition of the colonies cannot begin to take place before at least 16, and sometimes even 48, hours has elapsed.

Dr. McCracken takes issue with the tradition of utilizing Loeffler's medium for sure-fire verification of diphtheria. "A very old medium," he calls it, that "is not really good for diagnosis."

Even the standard tellurite plate—always recommended for use in conjunction with Loeffler's medium—is not as valuable as blood agar, according to Dr. McCracken, who is now at the University of Texas Medical School at Houston.

Blood agar's usefulness was twofold since it is also employed to diagnose beta-hemolytic streptococci. It turned out that 50 of the 201 San Antonio 1970 diphtheria inpatients had concurrent streptococcal infection—a finding especially noteworthy for physicians who do not suspect diphtheria if classic "strep throat" is present.

Dr. Mauney, in a separate interview, pointed out that unless physicians and technologists examining blood-agar colonies under a microscope are careful, they can mistake C. diphtheriae for Neisseria. "That's the main thing we have to distinguish C. diphtheriae from. We do it very simply by doing an oxidase test. If the organism is positive to the reagent—and

Neisseria is—it turns magenta color and then black. Neisseria is one of the few organisms that are oxidase-positive; in fact, it's about the only one in the mouth that is."

If the organism proves to be oxidase-negative? "We would go ahead further and do a gram stain," Dr. Mauney replied. "C. diphtheriae is a gram-positive bacillus; Neisseria is a gram-negative coccus."

According to Dr. Mauney, who is now at Charlotte (N.C.) Memorial Hospital, all three types of cultures—Loeffler, tellurite, and blood agar—together comprise "the best system you can find" for diagnosing diphtheria. "I'll stand up to that any day."

Although the tellurite is "absolutely useless" for visual distinction of C. diphtheriae—many organisms give rise to black colonies on it—the "garlicky" odor that organism has on it "is a very helpful thing," Dr. Mauney explained.

Loeffler's medium is valuable because, unlike blood agar, it stimulates metachromasia. Dr. Mauney continued. "Blood agar for colony morphology, Loeffler's for metachromasia, and tellurite for odor—then we'd do a nitrate test and a urease test. C. diphtheriae is urease-negative and nitrate-positive. That entire combination eliminates almost all of the nonpathogenic diphtheroids."

Nevertheless, a toxigenicity test was then carried out, the Elek test. A positive reaction, a white streak, usually takes place between 16 and 24 hours.

Of the 201 San Antonio cases of diphtheria in 1970, 144 were laboratory-confirmed. It is assumed for the other cases that antimicrobial therapy was instituted before swabs were taken. The intermediate biotype was most frequent, although gravis and mitis strains were also found.

As for Dr. McCracken's investigation of the feasibility of rapid laboratory identification of the disease: It showed that diphtherin can be laboratory-confirmed in a matter of hours. The technique? Immunofluorescence microscopy. When applied to throat swabs first incubated in growth medium for three to four hours, it gave results identical to those of bacterial culture—biochemical testing over 95 per cent of the time. "This method," Dr. McCracken concluded, "can be usefully and economically applied to the examination of large numbers of specimens during an epidemic."

One of the most interesting—and confounding—laboratory results was that, in the main, a bacteriophage type that has never before been described characterized the epidemic. While the epidemic was riding high, infectious head Dr. McCloskey wrote to two Rumanian physicians who use a special phage-typing technique asking whether they would be willing to identify strains of the San Antonio cases. An affirmative response was received from Drs. Alice Saragea and Paula Maximescu, of the Dr. I. Cantacuzino Institute of Microbiology, Parasitology, and Epidemiology, Bucharest. "We've got hundreds of strains that we've typed now," Dr. McCloskey relates. And for the most part they add up to a newly recognized type, named by Dr. Saragea—according to a scheme she has devised—as type K.

The most unexpected kind of knowledge emanating from the epidemic has to do with the treatment of glomerulonephritis. Yet it is only because of the occurrence of the epidemic that a new clinical approach to the disease has come about at the present time.

This is intriguing because glomerulonephritis is not a common complication of diphtheria. And in human beings, the serum sickness to which the antitoxin treatment frequently gives rise does not cause

kidney disease. Yet from a larger immunologic perspective the investigation carried out by immunology head Dr. Kniker was very germane. It was tied to a study of the prevention of serum sickness.

It all began for Dr. Kniker back in 1962, when as a pediatrician he undertook an immunology fellowship at Scripps Clinic and Research Foundation, La Jolla, Calif. Working under Dr. Charles G. Cochrane, he studied "how immune complexes do their dirty work." The kidney, Dr. Kniker points out, "is the main organ insulted by the circulating complexes."

He learned that the most important factor allowing deposition of the circulating antigen-antibody complexes is increased permeability of the vessel wall and that this increase is due to the release of such chemicals as histamine and serotonin from blood cells.

"When we removed platelets from rabbits—by administering antiserum to the platelets—the immune complexes circulating during the acute serum sickness that we had induced by an injection of bovine serum albumin did not deposit well."

More to the clinical point, serum sickness in the rabbit was found to be preventable by administration of potent antihistamine-antiserotonin drugs. They were very exciting. A breakthrough. It meant that serious immune disease in the human might be prevented without blasting the victim with drugs, like steroids and immunosuppressants, which render him susceptible to infections and cancer.

At the University of Arkansas Medical Center in 1965, Dr. Kniker extended the rabbit research to encompass chronic serum sickness, which in the rabbit leads to progressive glomerulonephritis. He wanted to find out: Can an antihistamine-antiserotonin drug prevent chronic glomerulonephritis? "The marvelous results of the study were that, by golly, in the drug-treated rabbits we largely prevented chronic glomerulonephritis."

But: The real test is to cure the disease once it's advanced—because that's the way the patient comes to the doctor."

Drug Given to Rabbits

So in a new, controlled rabbit experiment the drug was administered after the rabbit had developed severe disease. The results? "The nephritis in the animals who had not received the medicine continued to progress. But in treated animals it began to be ameliorated. Fantastic. The immune complexes ceased depositing, so that the animals were able to clean up the mess and bag it to heal."

What about human beings?

"In 1967, I began looking all over the world for a way to study if antihistamine-antiserotonin drugs given orally to humans who had immune-complex diseases would work," Dr. Kniker related. "Could it prevent disease, such as in the case of serum sickness, or make it go away, such as in the case of glomerulonephritis?" "In my research, the experimental model is the key to success. We decided that serum sickness itself, due to an injection of horse serum (such as in tetanus, diphtheria, or rabies), would be the ideal disease to study," Dr. Kniker related. "WHO and pharmaceutical companies with international enterprises for endemic or epidemic situations. 'We just didn't come up with anything.'"

Within a month after he became a fac-

ulty member of the University of Texas Medical School at San Antonio in September, 1969, "the chief pediatric resident, Dr. Fernando Guerra, and I realized that we had seen two cases of diphtheria," said Dr. Kniker. "We kept getting one or two cases a month. It appeared that this disease was somewhat endemic in the community. So we devised a research protocol in which diphtheria patients were to receive an antihistamine-antiserotonin compound from the fourth to the 16th day after antitoxin treatment—the period of risk—in a blind fashion. As we would accumulate data, which would take years and years, we would learn what I had been trying to learn all along."

Suddenly, "we were having several cases a week. Finally, dozens. Thank goodness we were not set—we already had a working protocol."

The protocol was quickly refined and modified to include adults.

137 Patients Treated

A total of 137 patients with a clinical diagnosis of diphtheria, and who therefore were given antitoxin (from which they could develop serum sickness), received either an oral antihistamine-antiserotonin compound or placebo. They were continually evaluated clinically by Dr. Guerra and Dr. Susan E. M. Richards (who succeeded Dr. Guerra as chief pediatric resident) as well as by Dr. Kniker; the blood and urine of these patients were continually studied by Dr. Kniker. If discharged prior to the sixteenth day, the patient was treated and followed as an outpatient.

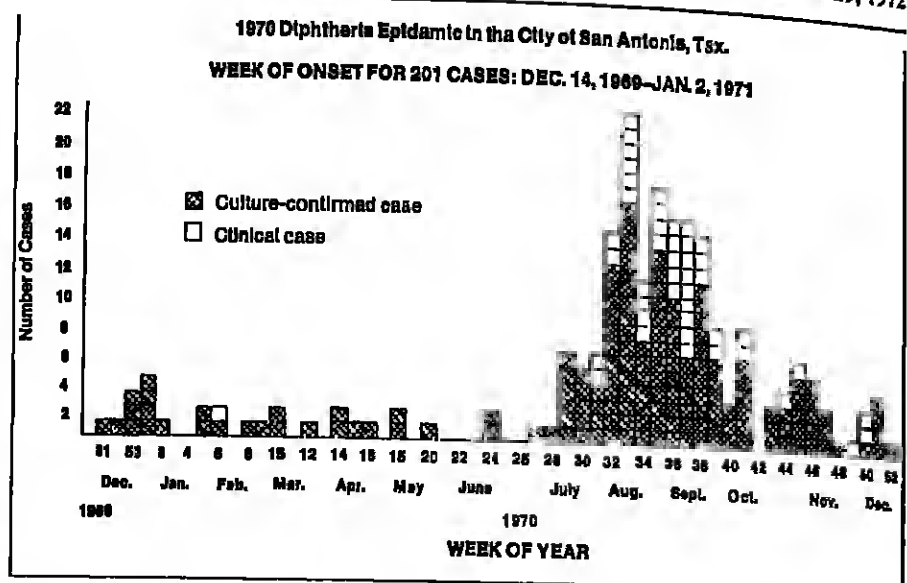
"What was terribly exciting for us was that only two diphtheria patients who took the antihistamine-antiserotonin compound developed serum sickness but that eight patients on placebo—28 per cent—did develop it. A difference of sevenfold. Moreover, the test drug had no side effects; it was well tolerated."

The Food and Drug Administration recently approved the use of the antihistamine-antiserotonin drug in the double-blind, collaborative study. The drug or a placebo will be taken orally round the clock for a year by patients with active, chronic kidney disease due to immune complexes for which consulting pathologists will do the biopsy studies to determine the nature of the disease in prospective study patients.

In addition to the University of Texas Medical School at San Antonio, the institutions now participating are Baylor College of Medicine, University of Arkansas Medical Center, University of Texas Medical Branch at Galveston, University of Texas Southwestern Medical School at Dallas, Wilford Hall U.S. Air Force Hospital, Brooks Army Medical Center, Veterans Administration Hospital, Little Rock, Ark., Scott and White Clinic, Temple, Tex., Veterans Administration Hospital, Oklahoma City, University of Oklahoma Medical Center, and Veterans Administration Hospital, Dallas.

"If we learn that this drug approach is efficacious," Dr. Kniker states, "then many forms of chronic immune diseases aside from the renal kind may be able to be approached in this way."

Results of antimicrobial therapy of patients and carriers will be among the learning sequelae discussed in the final installment.



Urban Dwellers May Be Unfit For Ski Slopes

Medical Tribune Report

SNOWMASS-AT-ASPEN, COLO.—Many persons leave their sedentary mode of life in the city and take to the ski slopes without adequate physical conditioning, sufficient warm-up, and even instruction, Dr. Fred L. Allman, Jr., Georgia Tech team orthopedist, said here.

"It is erroneous to believe that one can safely ski himself into shape," said Dr. Allman, who is also orthopedic consultant to Atlanta, Ga., public schools.

A prudent conditioning program for the skier must provide for progression until a high performance level or optimum fitness is achieved, he told a postgraduate course on skiing injuries, sponsored by the American Academy of Orthopaedic Surgeons.

"In order to improve performance, overload is necessary," he explained. "Overload is extending the work level beyond usual physical effort. This is achieved by exercising longer, or with greater intensity than usual, or both."

Skiing requires development of all parts of the body, Dr. Allman observed. Select an exercise program that will bring about cardiovascular endurance, muscular strength and endurance, and flexibility, he advised; ease into the program; be patient but persistent.

To avoid overexertion, be cautious about undue breathlessness and fatigue, inability to sleep, an elevated resting pulse, and prolonged soreness or joint discomfort, he said.

"Always warm up," Dr. Allman emphasized. "Calisthenics such as side-straddle hop and running in place are good warm-up exercises."

Dr. ALLMAN

Consistency Called Important

Duration of conditioning exercise should be at least 30 minutes, he said. Consistency must be adhered to if real value is to be obtained; otherwise, the activity must be considered a diversion. During the first month, if a person is woefully unfit, vigorous exercise should be performed every other day. As fitness improves, the workouts should be held at least five times weekly.

Select proper clothing and footwear, Dr. Allman continued. Clothing should be loose fitting and as light as possible. Footwear must be comfortable and the sole thick enough to offer a cushioning effect. Socks should fit well and should always be clean.

If overweight is a problem, a weight reduction diet should be followed, he said. Even if weight isn't a problem, a prudent diet should be encouraged.

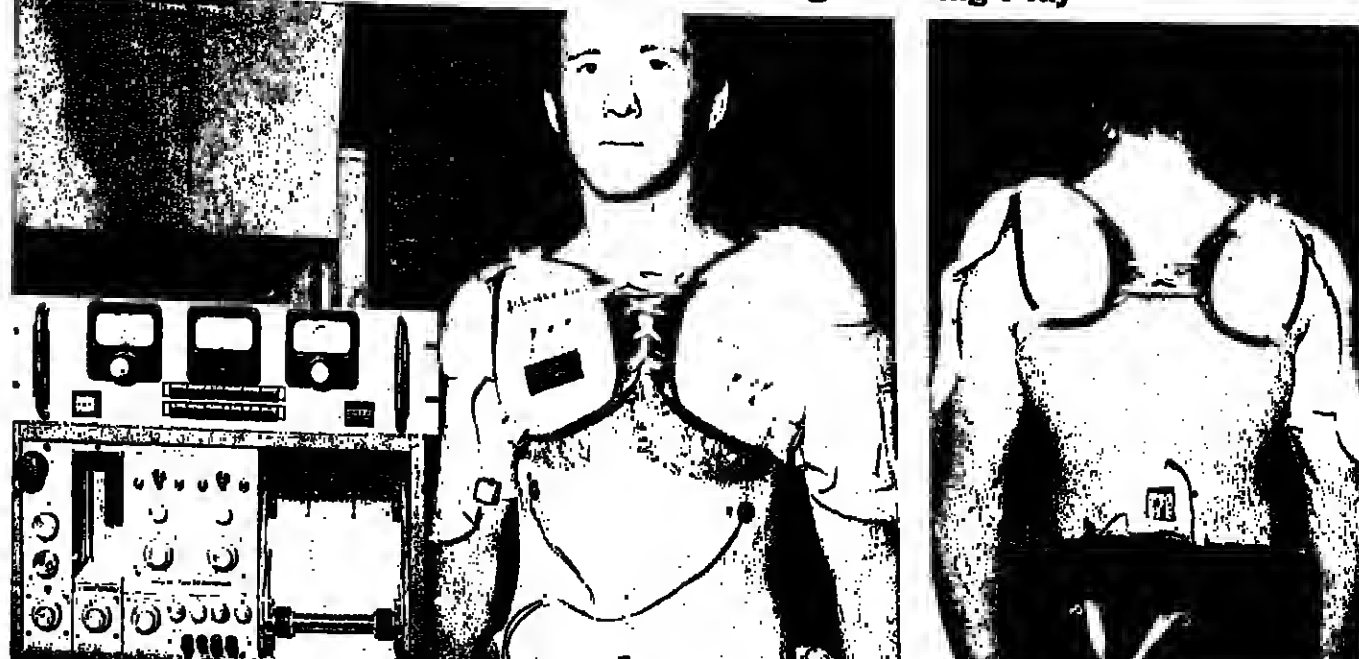
Rest and relaxation are a must, he said. One cannot have total fitness without the ability to relax at will. The recuperative effects of rest and relaxation are even more important to the individual who exercises vigorously than they are to the individual who remains inactive. The ability to relax completely usually requires a conscious effort, at least initially.

Keep records, he said. Record the quality and quantity, as well as the type of exercise performed daily. Periodically record vital body dimensions and other essential data. These records will note progress and help to provide motivation.

Dr. Allman spoke at a course on skiing injuries sponsored by the Committee on Sports Medicine of the American Academy of Orthopaedic Surgeons.

Dr. Allman spoke at a course on skiing injuries sponsored by the Committee on Sports Medicine of the American Academy of Orthopaedic Surgeons.

Hockey Players' Heart Rates Gauged During Play



Frontal and dorsal views of electrodes and transmitter placements used for radiotelemetry of heart rate during play in hockey game. Hematocrit and lactic acid blood concentration measurement and a videotaped time-motion study were part of experiment.

Circulatory Stress Held Usual in Hockey

Medical Tribune Report

PHILADELPHIA—A high degree of circulatory stress in ice hockey, with only slight declines in heart rate during periods of play stoppage, was reported by three Canadian investigators to the American College of Sports Medicine here.

They were H. J. Green, P. J. Bishop, and R. C. McKillop, of the Departments of Kinesiology and Athletics of the University of Waterloo in Ontario.

The study, of "one of the more accomplished" collegiate hockey players during a regular game, consisted of radiotelemetry of heart rate, measuring lactic acid concentration and hematocrit at the end of each period, and a time-motion study using a game videotape to determine length of shift, work and rest times, and average velocity.

The player, a star right winger, played a total of 1,207 seconds in 11 shifts on the ice. The presence of telemetry equipment and the drawing of blood samples did not appear to affect his performance, the investigators said.

During the player's shifts on the ice, the report said, work heart rate averaged 174 beats per minute, with a "rest" rate—while still on the ice—of 166 beats per minute. There was a considerable consistency among the heart rate values during shifts in all three periods of play. The average rate during the 36-second average work phase, according to the report, represented "approximately 90 per cent of the individual's maximal rate" as determined by a treadmill aerobic power test.

"Of significance as well," the investigators noted, "is that during the play stoppages, which amounted to an over-all average of 23 seconds, only a small drop in frequency was witnessed, indicating a maintained high circulatory stress throughout each shift."

Energy expenditure, calculated from the heart rate/VO₂ relation as determined by the treadmill test, was estimated at 75-80 per cent of the player's maximal aerobic power. This estimation, in the authors' opinions, however, "is very tenuous," especially since "erroneous approximations can result when trying to estimate energy expenditure for an activity other than that in which the heart rate/VO₂ relationship was established." Furthermore, they warned, the great amount of upper body activity in hockey "could serve to distort the relationship between these two variables."

Venous lactic acid concentrations were

high, indicating, the team concluded, "an appreciable contribution of anaerobic metabolism to the energy supplied." Lactic acid concentration, 134 mg. per 100 ml. in the first period, declined during the course of the game to 109 mg. per 100 ml. in the second stanza and 54 mg. per 100 ml. in the third.

Player Decreased His Speed

The lactate decline, the group hypothesized, may have been caused by a decrease in work output. Examination of the game videotape showed that the player, while playing longer shifts, did in fact decrease his speed during the third period. Hemocoagulation followed a pattern

similar to lactic acid concentrations. Hematocrit was 45 after the first period, decreased to 43 at the end of the second, and fell to the pregame level of 42 following the end of the game. The trend of hematocrit decrease ran counter to trends seen in other investigations, where hematocrit increased during heavy exercise, returning to pre-exercise levels during recovery. The Waterloo investigators theorized that "this could be a consequence of release of the large amount of water associated with glycogen storage which would lead to an elevated intratissular hydrostatic pressure and the decreased intracellular osmotic pressure associated with reduction in lactic acid concentration."

Fracture of the Fibula Shaft At Boot Top Common in Skiers

Medical Tribune Report

SNOWMASS-AT-ASPEN, COLO.—Fractures of the shaft of the fibula at the boot-top level was one of the most frequent injuries during the 1971-72 skiing season, Dr. Robert L. Swearingen, orthopedic surgeon at the Aspen Valley Hospital, said here.

"Every few years we see something new in ski injuries," Dr. Swearingen said. "Initially, with low, soft boots, it was lateral malleolar fractures and spiral fractures, then the new higher boots and boot-top fractures. Last year, we began seeing fractures of the shaft of the fibula at the boot-top level, primarily in adults but also in the older juveniles. This year, they have become one of our most numerous injuries. We have already verified more than 100 cases."

In explaining the mechanism of the injury, he said: "We have found that the new boots have aob an inner cant they throw the tibia into valgus compared to the old skis while the rigid boot sides tend to be in less valgus than the tibia. When an individual attempts to cut an inside edge, the rigid outer boot exerts force against the fibular shaft, and it cracks."

Dr. Swearingen reported on ailing fractures in children at a course sponsored by the Committee on Sports Medicine of the American Academy of Orthopaedic Surgeons.

In the past season, 189 fractures were seen at the Aspen Valley Hospital emergency room in patients between the ages

of four and 17, he said. This age group made up roughly 25 to 30 per cent of the total number of persons seen for ski trauma.

Of the 189 fractures, there were three skull and facial injuries, Dr. Swearingen said. One was a nasal fracture, one a comminuted mandibular fracture, and one a skull fracture that resulted in the death of a 16-year-old youth.

Two Spine Injuries Seen

There were two spine injuries—a mild compression fracture of the seventh thoracic vertebra and a mild compression fracture of the first and second lumbar vertebrae, he said. In the shoulder area, there were five fractures, and of four other injuries of the upper extremity, there was one distal radius and ulna fracture, two thumb metacarpal fractures, and one thumb phalangeal fracture.

The lower extremity fractures accounted for 175 of the fractures, Dr. Swearingen said. All of these were in some part of the tibia and/or fibula.

There were 56 fractures involving the shaft of the tibia with an associated fracture of the fibula, he said. These could be boot-top or spiral fractures, the aprils being usually at the junction of the middle and distal thirds. Fractures of the tibia shaft not associated with a fractured fibula accounted for 77 fractures. There were 10 fractures of the fibula shaft, these occurring much more frequently in the older age group. Twenty-two epiphyseal fractures occurred, seven malleolar fractures, and three miscellaneous, including an anterior tibial spine fracture and a plateau fracture.

Winter sports coverage will be continued in the next issue.



PROFESSOR GREEN



DR. SWEARINGEN

Growth Stocks Face Pension Fund Pressure

By ELIOT JANEWAY
Publisher of Janeway Service

PEACE-AND-PROSPERITY is no longer a magic formula that will start private accumulation of stocks again. Nor will it stop institutional distribution of blocks. Confusion between earnings results and money pressure problems has keyed the market up to its present state of hypersensitivity to earnings reports. The market has developed a silly-season response to any faltering in earnings progress by companies deservedly above suspicion. The distribution pressure intensifying the illiquidity problems plaguing the market from within reflect the need of a growing number of block holders to switch into high-yield securities or even to liquidate.

The next two years of labor negotiations and legislative reform will multiply the distribution pressures on institutional block holders. Paper profits will not satisfy the money demands or the statutory requirements about to be loaded onto the pension funds. Cashings in will become inescapable.

Switching proceeds into higher-yielding assets will become increasingly inescapable.

The latest reassurances about interest rates will not save the low-yielding growth stocks from the block liquidation which has started. Even if those of us who expect higher longer-term rates were proven wrong (and I more than ever doubt it), any decline in rates will be nominal: a drop to a 7 per cent yield basis would now represent real relief. The lightning up of the bond calendar is the main reason why bond market bulls expect lower rates; optimism about the lessening of inflationary pressures is their supporting reason. But the last time these conventional thinkers took a lightning calendar

as a guarantee of lower rates, they were forecasting a drop in a 6 per cent yield basis. Their present optimism represents negative progress. A reversal of the last move in a 7.5 per cent market would still leave the market saddled with a 7 per cent yield basis. This would leave the negative yield spread too wide to permit the pension funds to continue blithely and smugly to accept 1 per cent yields as the price for continuing to play the growth stock game.

The new terms coming in union retirement contracts and in mandatory funding conditions are forcing fiduciaries to jump the fence from growth to yield. It cannot be repeated often and emphatically enough that fiduciaries are motivated differently from individuals. Where individuals feel a keen personal incentive to question the value of the dollars they anticipate winding up with, fiduciaries are responsible only for paying out a fixed number of dollars on a fixed date—no matter what those dollars may be worth. Right now, the purchasing power of the future retirement dollar is the least of the worries haunting the fiduciary fraternity. Catching up with their unfunded deficiencies is immeasurably more bothersome. Getting fired by their clients for failing to avoid higher assessments from the actuaries is an even more pressing fear. The commotion that has started about earnings disappointments does not yet reflect the stepped-up charges the

actuaries are getting ready to load onto corporate contributions to pension funds. Of all the cost increases managements are now complaining about, none are more burdensome than the higher levies already required in their pension funds.

Utility stocks are the real beneficiaries of the bullish bond market forecast. They are outperforming the bond market. I think that they will continue to do so even after the confirmation of inflationary fears in the making again confounds the conventional thinkers who still equate the rise and fall of bond yields with the rise and fall of borrowing pressures on the bond calendar.

Reflects Magnitude of Shift

The upward bias reflected by the firming of the utility average reflects the magnitude of the switch from growth to income stocks. It is also building an oasis of technical strength throughout this specialized sector of the market because the utility stocks are the only ones attracting money from private individuals as well as from institutional block buyers. A parenthetical note on the always controversial question of how to read the breadth index is in order in connection with the upward bias of the utility stocks: there are enough of them benefitting from enough continuous daily buying pressure to give the advances and the unchanged columns a good head start on each day's performance. Using the realistic breadth index count—stocks up versus those not plus those unchanged (instead of the simplistic advances versus declines count)—argues for overruling the advances and unchanged column to exclude utilities (and possibly preferred stocks and closed-end bond funds). Substituting the high-yielding "mummy" stocks from the number of those advancing and remaining unchanged accentuates the distress of the groups where the daily declines are concentrated.

Changed response is now the order of the day on the stock market. The rise of illiquidity pressures is responsible for the switch. So long as the market was drenched in excess liquidity, good news was guaranteed to touch off buying waves. But now discretionary buying has given way to nondiscretionary selling—and that's always the worst kind. It has come to stay for the duration of the gap opening between pension fund obligations in future retirements and pension fund cash compounding. So long as this gap widens, news good enough to raise hopes for buying will be greeted as opportunities for selling. Consequently, the better the news, the more relentless the pressures of distribution will be. Not that the news will remain anything like as good as it now looks for very long. If good news is unable to help the market out of its present plight, what will help the market absorb the shock of bad news?

Sterling's collapse—it has been nothing less—is posing a puzzle for the metal markets, primarily copper. The normal response of the London-centered metal markets to a run on sterling is to take an off-setting jump. Sterling has already been

Zn, Cu Intake Studied



Researchers at the University of Cincinnati Medical Center led by Harold G. Peterling, Ph.D., have found a relationship in rats between serum lipid levels and the nutritional intake of zinc and copper. Study is financed by NIH.

marked down twice this year. But neither the winter devaluation nor the summer float produced an upward flurry of predictable proportions. Sterling's winter mark-down did coincide with a mild uptrend in the London copper market. But the drop resulting from the summer decision to float sterling failed to prevent a slide. This latest spell of weakness in sterling is not helping copper either.

Two related considerations have been fortifying the expectation that copper would hold its own against sterling being marked up more or less as much as sterling was marked down. The first consideration is sympathetic: all the grain markets are enjoying major hull market breakouts, reflecting fundamental long-term adjustments in sellers' market conditions. The other is arithmetic: copper has now been smudged down to levels at which it can be regarded as having bottomed out.

Copper Market Tolls Munch

I see no reason in retreat from my long-standing premise that the copper market is a reliable and, indeed, authoritative leading indicator of business, speculative, and financial market trends. The London copper market tells us more than we would otherwise know about these main trends, internationally as well as inside the principal market economies. All hands agree that the main drag on the copper market is the scheduled arrival on the market scene of the formidable new supply that has been in the pipeline these many years. The consequence of its coming on-stream is that merely nominal gains in demand will fail to prevent continued price weakness. This is the obvious and dispiriting prospect that the market has been discounting. It helps explain the unwillingness of the London Metal Exchange participants to reverse the persistent buildup in copper inventories.

MEDICAL MEETING SCHEDULE

Foreign Meetings

- Dec. 46 Chilean Society of Otorhinolaryngology Meeting, Santiago
- Dec. 56 Canadian Association for Research in Toxicology, Annual Symposium, Montreal
- Dec. 78 British Association of Plastic Surgeons, Winter Meeting, London
- Dec. 94 International Association of Biologists Standardization Symposium on Rabbits, Lyon, France
- Jan. 23-26 Canadian Association of Pediatric Surgeons, Annual Meeting, Toronto
- Jan. 28-30 U.S. International Foundation for Studies in Reproduction, North American Conference on Fertility and Sterility, Acapulco, Mexico
- Feb. 5-7 Association of Otolaryngologists of India, Bombay

- Feb. 16-18 Winter Medical-Dental Assembly, Prague and Tatra Mts., Czechoslovakia, and Budapest
- Feb. 21-23 American Medical Association and Wasmann Institute of Science Scientific Meeting, Tel Aviv
- Feb. 23-25 Central Surgical Association, Annual Meeting, Toronto
- March 6-10 International Exhibition and Technical Meetings for Medical Electronics and Biomechanics, Basel, Switzerland
- March 8-14 Minnequinia-MCW Medical Alumni Association Clinical Conference, Montego Bay, Jamaica
- March 10-15 International Conference on Group Medicine, Rio de Janeiro
- March 15-19 International Symposium on Reproductive Physiology, Tel Aviv
- March 21-31 Ceylon Medical Association, Anniversary Meeting, Colombo



Differential Diagnosis

Russell Baker, one of the nation's major assets, recently suggested in his "Observer" column in the *New York Times* that when the small irritations of life are grinding you to a pulp, it's a good idea to wallow in television commercials, where solutions to problems are instant.

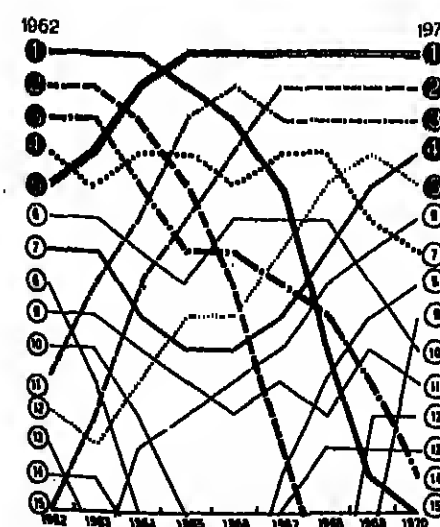
One of the several irritants that set him off was that his shower stall was leaking into the mashed potatoes on the dining-room sideboard. In televisionland, he writes, such catastrophes, as well as plumbers' bills "capable of reducing whole families to penury," are forbidden.

In our house the shower stall sporadically leaks through a cupboard onto mashed potatoes on a kitchen counter and has transformed part of the ceiling into an ominous-looking disaster area. Our problem, even before we get to those bills he mentions, seems to be finding out why the thing is leaking, and why sporadically. The solution begins with a battery of diagnostic tests that put to shame the average hospital admission procedure.

Is the floor plate, a mysterious, invisible thing under the tile floor of the stall, the culprit? To find out, we ended up performing that test ourselves. ("Might as well save yourself a few bucks," said the plumber, smirking openly over the bucks we eventually were not going to save.) To do a shower-stall floor-plate (SSFP) test, you plug the drain, fill the floor of the stall with water toed in from elsewhere, and wait an hour. If the ceiling doesn't leak, it's not the SSFP.

Successive tests were performed (by experts) on pipes-in-wall and faucets (a side effect of two cracked tiles turned up here), and what we're down to now is mildewed grout between tiles. So now we wait for the tile man. And wait.

Last time we complained to his office, his secretary gave us a one-word prescription, which we pass on to Russell Baker, if he wants it: "Bathe."



No, it's not a diagram of an intersection on the Los Angeles Freeway. It's a chart showing the relative market positions, since 1962, of the 15 top pharmaceutical companies that supply drugs to Britain's National Health Service. Our experience with it is that it's easier to admire than to understand. We found it in *New Scientist*, and they found it in an official report named "Focus on Pharmaceuticals."

"Now why does a person want to take his own life? Shakespeare put it well in Hamlet's soliloquy: 'To be, or not to be, that is the question.'"

—Diseases of the Nervous System. Thank goodness that's all cleared up.

Readers are invited to contribute items of 100 words or less to this column. Contributions should be mailed to MEDICAL TRIBUNE, 680 Third Avenue, New York, N.Y., 10022.

Lights

By JOHN E. McDEARMOTT, M.D.

"THE TRUCK just appeared out of the dark. I saw him too late. I couldn't stop."

Unfortunately, this patient is one of the few who can tell us the WHY of many nighttime auto crashes. The facts are simple: The sealed-beam headlight will not illuminate a sufficient distance ahead to allow 60-plus-mph driving. When envisioned in 1939, 75,000-candlepower sealed-beam system was quite adequate. Today, with more cars and higher speeds, the system is obsolete.

Sealed Beam vs. Bulb

Before the days of the sealed-beam headlight, the lighting systems of most vehicles were left to the manufacturers' devices and there was great variation. This fact, coupled with the average motorist's failure to keep the reflectors and inner lenses clean, led to the development of a foolproof unit. Such a unit, because of uniformity of design, could be mass-produced at a low cost and, when installed, easily aimed to the correct position. The sealed beam's introduction 30 years ago was a major milestone in auto safety and literally brought night driving out of the dark age.

Little has been done since this time to change the design or upgrade the thought on sealed-beam light systems in 30 years! We now find that the rest of the world has left us behind, saddled to this sealed-beam concept. This is not to say the sealed beam could not be changed, and perhaps this would be the most intelligent approach.

The so-called European system — employing separate bulb, reflector, and lens — has allowed the development of some uniquely designed lenses, which better protect the light out of oncoming drivers' eyes and onto the road. This, then, allows the use of much higher candlepower and increasingly efficient bulbs. Many who have traveled to Europe will recall seeing the square and rectangular headlights, often quartz iodine, used on European autos.

Quartz Iodine

The tungsten in the standard light bulb tends to burn and darken the outer surfaces of the bulb with use. By addition of iodine or halogen gas to the bulb, the tungsten can be caused to redeposit on the element itself; the bulb both burns brighter and will not darken with age. The quartz iodine or halogen lamps are more expensive and can be ruined if improperly handled, but their life is for all practical purposes as long as the standard light bulb. The answer could be sealed-beam quartz iodine lights with more scientifically designed lenses.

What can you do until the manufacturers are forced to put better lights on their

cars? Simply install driving lights. Most interstate buses and trucks use them, and you can well appreciate that Greyhound and others wouldn't equip their many thousand vehicles with such items unless they were worth it. Ranging in price from \$6 to over \$30, one can select any number of driving lights. They are available with either quartz iodine or standard-type bulbs and in a variety of sizes and shapes to fit most any-type automobile. The sole word of caution is that they are illegal in some states; some specify the type that can be used. However, most states literally lack laws governing the use of driving lights. The driving lights can be installed to work in combination with the high and low light switch of any car, as well as independently.

The driving lights should not be confused with the fog lights. Driving lights are usually clear in color and are designed to project a long-distance beam—a mile and a half, for the more powerful models.

Fog Lights

In contrast, the fog light, often amber colored, has a diffusing-type lens arrangement to enhance its fog penetration capabilities. The beam is designed to be diffused downward immediately toward road-side, rather than forward as in driving lights. Thus, it is apparent that the fog light would not work particularly well as a high-speed driving light, or vice versa. If you have ever driven an automobile with good fog lights in a fog situation, you will never want to grope without them. Again, a good lesson can be learned from interstate bus and truck operators.

Fog driving tips: In heavy fog switch on the flashers or drive with a turn signal on because being seen, particularly from the rear, is as important as being able to see.

Garage Grand Rounds

Most of us are familiar with the recall program by which manufacturers are instructed to recall certain models that have established defects. However, occasionally problems arise that though serious are not the nature of a true defect. "Consumer Protection Bulletins" are then issued by the National Highway Safety Commission. The unfortunate difference is, the majority of owners may be unaware of such con-

Check for Arrhythmias



Pinningpoint the location of cardiac arrhythmias, Dr. Andrew Wallace, Jr., and technician help surgeons correct disorder during open heart surgery on Wolf-Parkinson-White syndrome patient at Duke University Medical Center. W-P-W research at Duke is supported in part by an NHLI grant.

sumer protection bulletins, motoring merrily on their way unaware of potential danger.

1971-72 G.M. Cars

If you are the owner of a 1971 or 1972 General Motors automobile, except Cadillac—i.e., Pontiac, Buick, Oldsmobile, Chevrolet—you should be aware that the car has a potential of having sudden steering lockup. Stones or gravel becoming lodged in the steering control mechanism can jam the steering. The National Highway Safety Commission has warned in a "Consumer Protection Bulletin" that owners of these automobiles should drive at a "reduced rate of speed and with the utmost caution" immediately after traveling on a gravel road, as there have been repeated reports of rocks and gravel being trapped in the steering-joint area beneath the hood. The Safety Administration advises that G.M. dealers have been provided with gravel shields to be supplied to owners who have this problem or anticipate it. If you own a G.M. automobile of this vintage, 1971 to 1972, and use it for gravel roads, such a shield should be installed according to the Highway Traffic Safety Commission. "Car Clinics" advice is to put it on anyway, as gravel is a rather common contaminant of even our most superb urban street systems.

Pediatrician Gives Atherosclerosis Criteria

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premature myocardial infarction have shown elevated serum cholesterol levels.

"There are obviously some families in which heart attacks occur more frequently than would be expected," Dr. Blumenthal said. "This familial aggregation may be due to the fact that families usually consume the same sort of diet, have the same mode of life, and thus have much more in common than genes alone. But for a pediatrician, familial aggregation—no matter what the cause—is extremely important."

For those clearly identified as being at high risk, he stipulates that "appropriate advice" be given about exercise habits, diet, and the dangers of cigarette smoking. Treatment of biochemical disorders should be considered on an individual basis, in his opinion, and he advises caution in the management of infants "until we have more information about the possible hazards of drugs and diet therapy in the first years of life."

"relatively easily" at any time in the patient's first two decades of life, according to Dr. Robert L. Levy, of the National Heart and Lung Institute.

Dr. Levy, who is chief of the clinical service, Molecular Disease Branch, said that simple measurement of plasma cholesterol levels is often sufficient to detect this abnormal condition.

Diagnosis of type 2 hyperlipidemia has, in fact, now been made at birth in 29 infants by testing the cord blood, he reported. Each child was the offspring of a parent with such hyperlipidemia.

"This disorder is transmitted as a mendelian dominant trait," Dr. Levy said. "In the heterozygous state, it produces no other manifestation [than elevated levels of serum cholesterol] during the first two decades but it is associated with strikingly severe premature coronary artery disease in subsequent decades."

"The pediatrician must become a student of atherosclerosis," he said. "The presumption is now great that only by the early recognition, diagnosis, and treatment of disorders like type 2 hyperlipidemia can the current epidemic of coronary artery disease—the major health problem—be prevented or delayed."

Measuring Plasma Cholesterol Detects Type 2 Hyperlipidemia

From NHLI

► The type of hyperlipidemia known as primary familial type 2 can be recognized



DR. BLUMENTHAL